UNITED STATES DISTRICT COURT
FOR THE MIDDLE DISTRICT OF NORTH CAROLINA

Civil Action No. 1:22-CV-00101

WEI JIANG, M.D., Plaintiff, v. DUKE UNIVERSITY, DUKE UNIVERSITY HEALTH SYSTEM, MOIRA RYNN, M.D, in her individual and official capacity, and MARY E. KLOTMAN, in her individual and official capacity, Defendants.	)	**AMENDED COMPLAINT** **(Jury Trial Demanded)**

NOW COMES Plaintiff, Wei Jiang, by and through the undersigned counsel and complaining of the Defendants, says as follows:

NATURE OF THE ACTION

1. This is an action by Plaintiff under 42 U.S.C. § 1981 to correct unlawful and intentional employment practices including harassment, intentional discrimination, and retaliation by all of the Defendants against Plaintiff on the basis of Plaintiff's ancestry and ethnic characteristics, including her race, and to recover all damages permitted by law for the same.

2. This is also an action under Title VII of the Civil Rights Act of 1964, as amended, (42 U.S.C. § 2000e et seq.) to correct unlawful employment practices including harassment, discrimination, and retaliation by Defendant Duke University (Duke or DU) and Defendant Duke University Health System (DUHS) against Plaintiff on the basis of her race, national origin, color, and sex, and to recover all damages permitted by law for the same, including punitive damages under § 1981(a).

3. This is also an action under the Age Discrimination in Employment Act, as amended, (ADEA") (29 U.S.C. § 623 et seq.) to correct unlawful employment practices including harassment, discrimination, and retaliation by Defendant Duke and Defendant DUHS against Plaintiff on the basis of her age and to recover all damages permitted by law for the same.

PARTIES, JURISDICTION AND VENUE

4. Plaintiff was employed by Defendants Duke University (DU) and the Duke University Health System (DUHS) at the time of the acts alleged in this Complaint.

5. Defendant DU has been and is now a body politic and corporate, is capable of suing and being sued, and is located in Durham County, North

Carolina. Duke employed Plaintiff at all relevant times in this Complaint. It has delegated the authority to operate a non-profit health care system to Defendant DUHS as stated in Exhibit A to its Articles of Restatement filed with the N.C. Secretary of State's office on June 26, 2020, effective July 1, 2020. (**Exhibit 1, p4, § VI.B**.)

6. Defendant DUHS has been and is a body politic and corporate, is capable of suing and being sued, and is located in Durham County, North Carolina. According to Exhibit 1, "[t]purpose for which the Corporation is organized is to operate an integrated academic health system which will provide medical care, hospital care, medical education, and medical research through hospitals, clinical research organizations, affiliated physicians groups, outpatient clinics, managed health care plans, and other appropriate facilities and related entities, and through affiliations and other relationships with other health care and related service providers." In addition, "[t]he Corporation shall also provide support, financial and otherwise, to the medical and other educational and research activities of Duke University, a North Carolina nonprofit corporation, including without limitation the Duke University Medical School and other entities affiliated with Duke University." (**Exhibit 1, p3, § IV**)

7. Along with Defendant Duke, DUHS was a joint employer of Plaintiff at all relevant times in this Complaint.

8. Defendant Moira Rynn (Rynn) has served as the chair of the Department of Psychiatry and Behavioral Sciences at Duke and DUHS since 2017 and served as Plaintiff's supervisor since that time.

9. Defendant Mary E. Klotman has served as the Dean of the Duke University Medical School since July 2017 and is thus responsible for the supervision and management of Defendant Rynn and Plaintiff.

10. This Court has jurisdiction over Plaintiff's Title VII claim under 42 U.S.C. § 2000e5(f)(3) and 28 U.S.C. § 1331 and 42 U.S.C. § 1981a(a); Plaintiff's ADEA claim under 28 U.S. C. § 1331; and over Plaintiff's § 1981 claim under 28 U.S.C. §§ 1331 and 1343.

11. Venue is proper in this district in that the unlawful employment practices were committed in this district, the relevant employment records are maintained in this district, Defendants Duke and DUHS have their principal offices in this district, Defendants Rynn and Klotman and Plaintiff work in this district, and there is no other district that has substantial connection to the claim.

12. All conditions precedent to the institution of this lawsuit have been fulfilled, including the filing of a charge and the receipt of a right to sue letter from the Equal Employment Opportunity Commission.

STATEMENT OF FACTS

13. All allegations of each paragraph of this Complaint are incorporated into each Count thereof, as though fully set out therein.

14. Plaintiff was employed by Duke on Sept 1, 1989, as a Research Associate. She began a Formal Residency training on July 1, 1997, with the Duke Medicine & Psychiatry Combined Training Program. On July 1, 2002, she was hired at a salary of $105,000.00.

15. Over the years, Plaintiff was consistently promoted, her salary increased every year (except 2012 due to university financial constraints), and she was eventually awarded tenure as a Full Professor in 2014.

16. From 2004 through 2017 Plaintiff took annual and sometimes bi-annual trips to China to collaborate with colleagues, provide mental health outreach and attend and present at conferences. She also visited with family on these trips.

17. As of 2017, Plaintiff was seeing patients in a clinical practice, but

primarily was a researcher managing a laboratory at Duke and conducting clinical studies funded by grants from the National Institutes of Health (NIH) and the National Heart Lung and Blood Institute (NHLBI); these grants were for multiple years and funded a large portion of Plaintiff's salary. During her years of employment with Defendants, Plaintiff developed a strong reputation as a researcher, collaborator, and presenter unlike Defendant Rynn who resented her for the same, and who is not a tenured professor.

18. From September 2006 to November 2011, Plaintiff worked primarily on the REMIT study (Responses of Myocardial Ischemia to Escitalopram Treatment) (ClinicalTrials.gov Identifier NCT00574847), funded by the NHLBI which was designed to study, as its name suggested, the effects of the drug escitalopram on patients with myocardial ischemia (reduced blood flow to the heart which can result from conditions including mental or physical stress).

19. The earliest version of the study summarized the goal of the study as follows:

> **Brief Summary**: Depression is commonly seen in patients with cardiovascular disorders, as in recent studies it has been shown that mild to moderate depression symptoms were associated with increased likelihood of mental stress-induced myocardial ischemia (MSIMI), which is a risk factor of poor cardiac outcome. In this project, we aim to assess the treatment of mental stress-induced

myocardial ischemia in ischemic heart disease patients with mild to moderate depressive symptoms. This study is a six-week double-blind placebo-controlled study to examine the effects of escitalopram on **mental stress-induced myocardial ischemia**. This study will look to show that patients with ischemic heart disease who are treated with escitalopram will exhibit a significant improvement of **MSIMI** at the end of week 6 compared to patients receiving placebo.

Detailed Description: The goals of this project are to investigate the response of **mental stress-induced myocardial ischemia (MSIMI)** to escitalopram, an SSRI; to determine whether **MSIMI** will be reduced by the treatment, and whether the modification of **MSIMI** is related to improvement of depression symptoms, and/or to reduction of platelet aggregation, and/or to reduction of cardiovascular reactivity. This is a randomized study using escitalopram versus placebo for stable ischemic heart disease patients with **MSIMI**. This study will also explore the role of platelet activity in occurrence of **MSIMI** and other characteristics of **MSIMI**, such as systolic and diastolic function of the left ventricle during mental stress testing as comparing to exercise testing.

20. The final version was exactly the same but added one paragraph to the "detailed description":

The stress testing will be conducted at the Duke Cardiology Diagnostic Unit Laboratory. Following a 20-minute calibration-rest period, participants will be asked to complete a series of 3 **mental stress** tasks. There are 3 mental stress tasks to be used for this study, i.e., (1) Mental arithmetic: during this test, patients will be asked to perform a series of serial subtractions beginning at a given number which will be different for each repeated test and will be chosen by the tester from a fixed list of various numbers, with encouragement to perform calculations as quickly

> as possible; (2) Public speaking with anger recall: during this test, patients will be asked to give a speech on a recent situation in which they experienced anger to an audience of observers (two to three) after 1 minute of preparation. Prior to the speech, subjects are told that their speech will be evaluated on their description of the situation, as to what happened, what they thought, felt, what they did, and what happened as a result. If they run out of things to say, the research tech will prompt them with questions to elicit more content until the three minutes are up; (3) Mirror trace: during this test, patients will be asked to outline, as quickly as possible, a star from its reflection in a mirror. Each task will last 3 minutes and there will be a 6-minute rest period between tasks.

21. The last version reported the outcome measures. The primary outcome measure listed (number 1) was entitled "Percentage of Participants With an Absence of **Mental Stress-induced Myocardial Ischemia** (**MSIMI**) During the 3 Mental Stressors." Number 2 on the outcome measures, described as "primary," was entitled "Percentage of Participants With Overall **Mental Stress-induced Myocardial Ischemia (MSIMI)**."

22. Significantly, in version 9, the last version, outcome measures 3 – 14, were all labelled secondary outcomes and only the very last one, number 14, made any reference to "Exercise Stressed-induced Myocardial Ischemia (ESIMI)). Evaluation of ESIMI was not the primary focus of the REMIT study.

23. The REMIT study investigators published a paper in the American Heart Journal in 2012 describing the research methods for the study being

conducted:

> Substantially accumulated evidence demonstrates that transient emotional distress or **mental stress** is strongly linked to coronary heart disease (CHD).1 Over the last couple of decades, the association of mental activity and myocardial ischemia has been well studied. **Mental stress–induced myocardial ischemia (MSIMI)** in the laboratory may occur in up to 70% in patients with clinically stable CHD2 and is associated with increased death and cardiovascular (CV) events. Few studies have examined therapeutics that effectively modify **MSIMI**. We, therefore, are conducting a clinical trial, that is, the REMIT trial, to investigate whether selective serotonin reuptake inhibitor (SSRI) treatment can improve **MSIMI**. The methods and rationale of the study are described.

Clearly, and significantly, the focus of the study as described in this article was on **MSIMI**, not ESIMI.

24. The REMIT study investigators published a paper in 2013 in the Journal of the American Medical Association (JAMA) in which they reported statistically significant results regarding **MSIMI** (more patients taking escitalopram had an absence of **MSIMI** during the 3 mental stressor tasks compared with patients taking the placebo) based on the unadjusted multiple imputation model for intention-to-treat analysis. The JAMA article also noted that rates of ESIMI were slightly lower in the escitalopram group than in the placebo group, but significantly acknowledged that the difference was not

statistically significant.

25. A total of six papers were eventually written about the REMIT study and its conclusions. More papers could have been written but for Defendants' actions in sabotaging Plaintiff's research and publications career, as detailed herein.

BEGINNING OF THE AUDITS OF THE REMIT STUDY

26. After the JAMA publication in 2013, years passed.

27. On July 1, 2017, Defendant Rynn was hired to be the chair of the Department of Psychiatry and Behavioral Sciences. At his time, Plaintiff was earning over $200,000.

28. Plaintiff's salary had consistently increased since her initial employment with Defendants Duke and DUHS. Specifically:

DATE	SALARY
July 01, 2003	$125,000.04
July 01, 2004	$128,450.04
July 01, 2005	$132,000.00
July 01, 2006	$140,000.00
July 01, 2007	$144,900.00
July 01, 2008	$150,405.96

October 01, 2009	165,456.00
March 01, 2010	$173,728.80
July 01, 2011	$178,940.64
July 01, 2012	$178,940.64
July 01, 2013	$182,519.40
July 01, 2014	$186,169.80
July 01, 2015	$190,824.00
July 01, 2016	$195,594.60
July 01, 2017	$200,484.48

29. Defendant Rynn was selected as Chair of the Defendants Duke and DUHS Psychiatry and Behavioral Science department on July 1, 2017.

30. On April 18, 2018, Defendant Rynn requested an audit of the REMIT study for which Plaintiff was assigned as Principal Investigator.

31. As of July 1, 2018, Plaintiff's salary was reduced to $152,629.92.

32. As of July 1, 2019, Plaintiff's salary was reduced to $34,418.00, where it has remained since that time, despite the fact that other non-Asian, male, and younger physicians have been hired by Defendants since that time at much higher salaries for comparable work.

33. In the most three most recent annual appointment letters provided to Plaintiff by Defendant Rynn, Rynn had no discussion with Plaintiff as opposed to other faculty members, whose names have not yet been discovered, but will be identified as John Doe, Jack Smith, and James LNU, who were similarly situated to Plaintiff but not older, Asian, and female.

34. The letters to Plaintiff stated only that Plaintiff would be working in a full professor position at an annual salary of $34,418.00. A newly hired faculty with "instructor" position in 2020 earned an annual income of $220,000.00. The difference in the salary paid to Plaintiff and the salary paid to John Doe, Jack Smith, and James LNU is attributable to discrimination based on Plaintiff's race, age, sex, and national origin.

35. Plaintiff has a distinguished career as a researcher with many published articles and is a tenured professor and is older than Rynn. **Exhibit 2.** In addition, English is her second language; she speaks with an Asian accent.

36. Defendant Rynn is not a tenured professor, and her research career pales in comparison to Plaintiff's. **Exhibit 3.** Rynn is younger than Plaintiff and English is her first language, and she does not speak with an Asian accent.

37. Beginning in 2018, Defendant Rynn, with the oversight and approval of

Defendants DU and DUHS, began a campaign to disparage the REMIT study, and primarily Plaintiff's involvement in it as Principal (but not sole) Investigator. This disparagement was intended to cast doubt on Plaintiff's abilities to administer grants and serve as a principal investigator.

38. However, the scrutiny instigated by Defendant Rynn extended beyond a routine audit of a grant and evolved into Rynn's questioning the data analysis and conclusions reached in articles published not by just Plaintiff but co-authored by her co-investigators.

39. This scrutiny by Rynn and the other Defendants constituted discriminatory practices based on Plaintiff's race, sex, national origin, and age, and due to Rynn's professional jealously of Plaintiff as an accomplished researcher and tenured professor, which Rynn was not.

40. Plaintiff was out of the country in April 2018. While travelling in China in April 2018 performing outreach activities to medical colleagues and visiting family, Plaintiff saw that Scott Kollins was stepping down as Vice Chair for Research and Plaintiff reached out to Defendant Rynn and expressed in interest in the position. Rynn did not respond.

41. During this same time Plaintiff was out of the country, Defendant Rynn

instigated an internal review of the study files for the REMIT study. Rynn assigned Sharikia Burt, the Assistant Research Practice Manager, to conduct the review. Burt began the study by scheduling an interview with Pamela Bonner, Plaintiff's research coordinator for her lab since 2017.

42. Unbeknownst to Plaintiff at the time, Rynn had called Bonner to her office to discuss Plaintiff's lab practices and thereafter used that meeting as a justification for beginning the multiple reviews that ensued into the REMIT study.

43. When Plaintiff returned to the country and to her office on April 25, 2018, she consulted with Dr. Jeannie Beckham about the reason for the departmental audit of the REMIT study which was by this time ongoing.

44. Beckham told Plaintiff that Pamela Bonner had made a complaint to Defendant Rynn alleging that Plaintiff did not know how to manage a laboratory. Plaintiff was shocked and wanted to reach out to Bonner, but Beckham instructed her not to discuss the matter with Bonner in order to not be viewed as retaliating against Bonner.

45. On April 30, 2018, Defendant Rynn requested a meeting with Plaintiff and indicated that she wanted to follow up the departmental audit with an

audit by the university audit office. Rynn told Plaintiff that the audit would be a good way for Plaintiff to improve her research.

46. Plaintiff did not suspect any ill motives by Rynn at this time and although she did not understand why Rynn would want to revisit a study that had concluded in 2015, she did not oppose Rynn's desire to have the study audited past the departmental level. Rynn treated Plaintiff differently based on her race, sex, national origin, and age, and she instigated no other such audits of researchers similarly situated to Plaintiff.

47. Significantly, Plaintiff was provided no opportunity by Defendant Rynn to respond to the first Clinical Research Unit (CRU) report authored by Burt.

48. After her meeting with Plaintiff, Rynn then emailed Leigh Goller and David Falcone of the university Office of Audit, Risk, and Compliance (OARC) and indicated that Plaintiff and Rynn were requesting that the university audit the REMIT study.

49. After this email from Rynn, Falcone sent an email on May 1, 2018, asking Plaintiff or Rynn to call him, but later that day Rynn emailed Plaintiff and told her that there was no need for her to reach out and that Falcone had told her that his team would meet with her in 2-3 weeks.

50. Plaintiff would later observe, as the audits of the REMIT study continued, that Rynn would often essentially attempt to "run interference" and prevent Plaintiff from contacting individuals who were involved in Rynn's efforts to discredit the REMIT study.

51. James Blumenthal, J.P. Gibbons Distinguished Professor of Psychiatry, confirmed that Rynn's practice of preventing Plaintiff from discussing the audit matters was unusual.

52. Also on May 1, 2018, as previously scheduled prior to Plaintiff's trip to China, Pamela Bonner left Plaintiff's lab.

53. On May 3, 2018, the departmental audit instigated by Defendant Rynn while Plaintiff was in China was completed and the report issued by Sharikia Burt stated that a departmental recommendation was being made to "escalate" the study "[d]ue to various issues observed during the QA review that may affect data integrity, subject safety and the concern for proper PI oversight."

54. Curiously, this report dated May 3, 2018, postdated Rynn's discussion with Plaintiff about elevating the audit of the REMIT study to the university audit office to which she attempted to get Plaintiff's consent. Thus, it appears that Rynn was managing the departmental audit report from behind the

scenes and was successful in having included in the departmental study a recommendation to "escalate" the audit of the study to the university level.

55. The OARC Research Compliance Assurance (RCA) visited the research offices where the REMIT study records were kept between June 4-13 and July 3-7, 2018. They reviewed only 17 out of 310 subject study records initially and then 8 more after initial review.

56. After the REMIT study, Plaintiff submitted another grant request to the NHLBI. NHLBI indicated in early July 2018, that it needed Plaintiff's response to the "just in time" (JIT)[1] document issued by agency. The departmental Clinical Research Unit (CRU) was responsible for providing the JIT response. The JIT eventually was prepared, but its delay caused significant tension.

57. Plaintiff reached out to Defendant Rynn and learned for the first time that Rynn had chosen not to fill the CRU director position or the Vice Chair for Research position about which Plaintiff had inquired in April which was vacated by Scott Kollins. Instead, Rynn had decided that she would serve as the interim CRU director. Thus, the delay in getting the JIT document was the

[1] JIT documents are used by federal agencies to request pre-award materials that were not submitted as part of the original grant application.

result of the fact that Scott Kollins had not been replaced as CRU head, which Plaintiff explained to the program officer at the NHLBI and copied Rynn in an email on August 21, 2018.

58. Rynn then scheduled a meeting with Plaintiff and Plaintiff learned that Rynn was going to supervise the CRU, and not replace Scott Kollins, and that she was offended by what she considered Plaintiff's criticism of the CRU's failure to submit the JIT response to the NHLBI program officer.

59. On September 10, 2018, the Office of Audit, Research, and Compliance (OARC) Research Compliance Assurance (RCA) issued a report based on its review of 25 of the 310 subjects of the REMIT study and noted no significant patient safety concerns. Protocol and documentation concerns were noted, and the RCA recommended that Plaintiff and the study team submit the OARC report and Plaintiff's response to the university Institutional Review Board (IRB). The OARC also indicated that it had discussed the recommendations regarding protocols and "good clinical practices" (GCP) with both the IRB and the Duke Office of Clinical Research (DOCR) and the OARC was leaving implementation of its recommendations "to the discretion of the IRB and Psychiatry leadership."

60. The RCA recommended that the "IRB consult with a statistician to evaluate if and how data quality issues impact existing and future publications."

61. The OARC issued a report noting no patient safety concerns, but issues with protocol adherence. However, the protocol adherence issues turned out to be related to the exercise stress testing inclusion/exclusion criteria, which was not the primary focus of the study; the primary focus of the study was mental stress IMI, not physical stress IMI.

62. In addition, the OARC RCA made recommendations for changes in the REMIT study, apparently unaware that the REMIT study had concluded more than three years prior to the OARC RCA's review and many of the recommendations could not be implemented retroactively but only prospectively in future studies.

63. On September 20, 2018, Bonner wrote Plaintiff asking her to be a reference for Bonner. Confused about why Bonner would want a reference from her if she believed that Plaintiff was a sub-par investigator, Plaintiff reached out to Bonner to schedule a meeting which occurred on September 24, 2018.

64. At this meeting, Bonner informed Plaintiff that she was called in to

Defendant Rynn's office (the Department Chair) and Defendant Rynn "grilled" her for about an hour about the work done in Plaintiff's lab. Bonner told Plaintiff that she never stated that she had problems with Plaintiff's lab.

65. On September 25, the next day, Bonner wrote Plaintiff an email stating:

> I'm sorry that you were told all these things and asked not to discuss them with me. I don't remember saying that I would not want to work with you again at that meeting, and I don't feel that way. Hopefully, we can keep our communication better in the future. I know that I told them that I thought you were genuinely trying to follow the rules that you knew about and that it seemed like the issues that I had noticed were from no one telling the study team about evolving best practices. When asked about data integrity, I told them that I felt that your data could be trusted, that you have a great deal of personal integrity, and that any issues were only ones of documentation practices. I recommended more training for all the CRCs in the department and more guidance/support for the principal investigators. I did recommend that they give you an experienced CRC to work with in the future if you were funded for your study. I hope that you still feel good about me after all this hearsay, and I do hope for the best for your new projects moving forward.

66. Defendant Rynn's pretextual reliance on Bonner's complaints as a basis for the reason for auditing the REMIT study thus became obvious to Plaintiff and Plaintiff became concerned that Rynn was targeting her by continuing to mislead her about escalations of what were minor audit issues.

67. On the same day that Plaintiff met with Bonner, she learned that her

grant for NHLBI project R01, R01HL140060 designed to examine "Mental Stress-Induced Left Ventricular Dysfunction and Mitochondrial Dysfunction in Women" was awarded for a period for 4 years. On Plaintiff's original proposal. The initial year alone was funded at almost $800,000.00.

68. Between October 4 and November 1, 2018, Plaintiff travelled to China on an outreach trip and to visit her family.

69. The OARC RCA report was submitted to the IRB on November 26, 2018, and evaluated by the IRB on December 19, 2018. The IRB concluded that there the report did not show any Involving Risk to Subjects or Others (UPIRTSO). The IRB concurred with OARC recommendations, presumably made with regard to prospective studies given that the REMIT study had long concluded. As to the REMIT study, the IRB stated it wanted to see independent expert opinion on the "interpretation of the stress tests, ECHOs and how the ineligible patients were handled in the reporting of the data." The IRB stated that the "**PI and Investigators**, **with the support of the CRU and School of Medicine, should seek independent expert opinion on these issues and report back to the Board with their conclusions**."

70. Despite this IRB request, not only did Defendant Rynn not support the

acquisition of an independent expert to resolve any outstanding issues about the REMIT study.

71. Instead, Defendant Rynn instigated a second departmental Clinical Research Unit review of the REMIT study, decidedly not independent, and focused on the inclusion/exclusion criteria applied to 127 of the original 307 patients who completed the REMIT baseline screening and were found to have met the "eligibility criteria" for the study.

72. Again, Defendant Rynn's scrutiny of Plaintiff's involvement in the REMIT study in which many other researchers were involved centered on Plaintiff.

73. The CRU review was conducted by Terry Ainsworth, Director of Research in the DOCR; Alifia Hasan, the departmental research practice manager for the Psychiatry department; and Scott Compton, who had been selected by Defendant Rynn finally to become the Director of the Psychiatry CRU.

74. The CRU focused primarily on changes to the exclusion criteria in the original protocol which were made to ensure patient safety.

Table 2. A Summary of the Number of Participants that Failed by Eligibility Criteria		
Eligibility Criteria	**Number of Participants**	**Participant IDs**
EC 1 Recent myocardial infarction, coronary artery bypass graft surgery, or other revascularization procedures (>3 months)	N = 1	090-024
EC 4 Unable to withdraw from anti-anginal medications during ischemic assessment phase	N = 10	161-049; 175-054; 206-066; 233-077; 235-080; 238-082; 264-089; 299-098; 310-105; 358-115
EC 5 Unable to perform exercise testing	N = 6	020-004; 046-016; 102-029; 180-051; 236-081; 377-121
EC 6 Pregnancy	N = 3	109-033; 319-103; 379-122
EC 10 Significant cardiac, pulmonary,	N = 1	025-012

Table 2. A Summary of the Number of Participants that Failed by Eligibility Criteria		
Eligibility Criteria	**Number of Participants**	**Participant IDs**
metabolic, renal, hepatic disease, or malignancy, interfering with patient's participation in this study		
EC 12 currently taking anti-depressants that can not be discontinued	N = 1	144-042
IC 3.1 and EC 4 ***(IC dropped as of 10/2008)*** and Unable to withdraw from anti-anginal medications during ischemic assessment phase	N = 1	015-003
EC 4 and EC 5 Unable to withdraw from anti-anginal medications during ischemic assessment phase and Unable to	N = 2	268-093; 284-095

Table 2. A Summary of the Number of Participants that Failed by Eligibility Criteria		
Eligibility Criteria	**Number of Participants**	**Participant IDs**
perform exercise testing		
EC 6 and EC 12 Pregnancy & currently taking anti-depressants that can not be discontinued	N = 1	265-090

75. EC 4 (unable to withdraw from anti-anginal medications) and EC 12 (currently taking anti-depressants that cannot be discontinued) were waived for 15 study participants to allow the study participants to safety continue participation in the study. Because the study evaluated patients at baseline on medication and then at the conclusion of the study on the same medication, waiving these exclusions had no effect on the study's conclusions about mental stress IMI.

76. EC 5 (unable to perform exercise testing) was also waived for six participants to allow the study participants to safety continue participation in the study. In addition, because exercise stress IMI was not a primary focus of the study, waiving this exclusion criterion has no effect on the conclusions

about MSIMI.

77. One patient was allowed to participate despite his undergoing a cardio-diagnostic cardiac catheterization on June 30, 2008, because he had chest pain symptoms. The patient was found to have no acute myocardial infarction. He had no re-vascularization and was found to have normal LV function. Ultimately, his cardiologist informed the REMIT study investigators, which included cardiologists, that the patient's IHD was stable, and he agreed to have the patient enrolled in the REMIT study. Thus, there was no patient safety concern.

78. One participant in the study was not excluded because 6 days after baseline testing he was ultimately diagnosed with a "significant cardiac, pulmonary, metabolic, renal, hepatic disease, or malignancy, interfering with patient's participation in this study" (EC 10), that diagnosis did not occur until after baseline testing and randomization to the REMIT intervention and there was no evidence that he had cancer prior to a dizziness episode which occurred after randomization.

79. Again, most of the questions about the inclusion and exclusion criteria related to the cardiovascular health of the patients. Instead of consulting with

the cardiologists' investigators on this study, Defendant Rynn attempted to hold Plaintiff responsible and treated her differently because Rynn treated Plaintiff differently because of her race, sex, national origin, and age.

80. On December 18, 2018, Geeta Swamy sent Plaintiff and email stating:

> The SOM is wanting to get a full understanding of your most recent trip to China- what was the nature of the trip- was there any funding provided to Jan – including the cost of her travels etc. The SoM has recently received a letter from NIH regarding a PI in another Department who failed to note that he had collaborated internationally with China etc. Geeta and team remembered that you had recently traveled and wanted to find out the details of the trip to be sure we don't need to disclose anything on her behalf.

81. On January 7, 2019, Plaintiff met with Defendant Rynn and suggested that because the new grant also involved cardiologists that the grant might be better supervised out of the cardiology department. Rynn apparently perceiving this as a threat, then threatened to terminate the grant under her authority as Department chair.

82. At this same time, Plaintiff sought again to obtain CRU and departmental support for complying with the IRB request that the Plaintiff and her Investigators, with the support of the CRU and School of Medicine, seek "an independent expert opinion on these issues and report back to the

Board with their conclusions." Rynn instructed Plaintiff that she was not permitted to discuss the ongoing audits with her co-investigators.

83. Rynn held Plaintiff responsible for the entire conduct of the study and all decisions made with regard to the study, as opposed to addressing issues to all of the investigators or allowing Plaintiff to do so.

84. Scott Compton told Plaintiff he would reach out to the IRB about whether a random sample of the ECHOs and exercise stress tests could be evaluated and relayed on January 9, 2020, and that Jody Power with the IRB had said that a random sample would be fine, but that a "deeper dive" might be required at some point.

85. Plaintiff then told Compton that she was going to confer with her co-investigators as directed by the IRB. Compton then sent Plaintiff an email copying Defendant Rynn stating that "Moira expressly asked that we not discuss the audit with anyone outside of Duke. . . . Based upon this request, I think it would not be prudent to inform the cardiologists at this point in time." Defendant Rynn responded to the email stating: "That is correct, Scott, no one has my permission to share any information pertaining to this audit outside of our group. Thanks, Moira."

86. Plaintiff then wrote an email to both Compton and Defendant Rynn stating:

> having a hard time comprehending why I cannot communicate with the co-investigators of REMIT about the audit. They have been working with us for many years and have made unique contributions to REMIT study. From the Echo standpoint, as the PI of REMIT, except for outlining guidelines, I have no role in the REMIT echo quality and interpretation process. I feel that it would be respectful to my echo-cardiology collaborative colleagues, who reviewed all the REMIT echo images, that their echo ratings will be re-examined. Dr. Eric Velazquez and Dr. Zainab Samad are very well known echo-cardiologists who have had top level echo training. They also have enriched experience in analyzing mental stress induced cardiac echo images. I think they may have adjunct positions with Duke after they moved to Chairs of Medicine in different institutions. I sincerely think they need to be informed of the decision to re-read the echo images.
>
> Moving forward, I would like to make a suggestion. Given the nature of cardiac echo imaging study and the unique hemodynamic impact of mental stress on cardiovascular system, it would be a good idea to have echo-cardiologists who have had comparable training and experience with mental stress testing to do the required re-rating.

Plaintiff received no response to this email.

87. Meanwhile, the second CRU report instigated by Defendant Rynn was sent to the IRB on January 18, 2019. This time, Plaintiff was given an opportunity to provide her response to the report and she did.

88. On February 25, 2019, Jiang received email messages from her

department CRU and the Duke Office of Scientific Integrity - COI Faculty Correspondence, asking her:

> Lindsey Spangler, from Research Facilitation, has reached out to me to make sure that you contact COI regarding your travels to China. She wanted to make sure that you have reported these activities correctly. Can you please promptly reach out to them and let us know when this has been completed. The Duke COI office can be reached at (919) 684-312.

89. In a shocking escalation of the hostile work environment to which Plaintiff had been subjected, on January 23, 2019, at a meeting with Plaintiff and Geeta Swamy, Defendant Rynn informed Plaintiff that in her capacity as Department Chair, Rynn had decided to terminate Plaintiff's grant which had been awarded in the Fall of 2018.

90. Dr. Blumenthal was shocked when he learned that Rynn had cancelled Plaintiff's grant. In the 50 years he has been working, he had never seen such obviously unfair and hostile treatment, especially given the reasons for the cancellation of this grant. He had never heard of this happening to any other colleagues, including non-Asian male younger or any colleagues.

91. This grant had a first-year value of almost $800,000 and would have provided valuable research as well as financial support for Plaintiff's career.

92. This termination occurred in complete non-compliance with the IRB

procedures for terminating previously approved research protocols. This termination was an adverse action clearly based on Plaintiff's race, sex, age, and national origin, was unprecedented, and another example of how Plaintiff was treated differently from other researchers who were similarly situated to her except as to race, sex, age, and national origin. The reasons given for the cancellation were completely out of proportion to the actual action taken.

93. No other IRB approved protocols have been terminated in the same manner as Plaintiff's, including white male researchers John Doe, Jack Smith, and James LNU. Plaintiff was singled out by Defendant Rynn and treated differently based on Plaintiff's race, sex, national origin, and age.

94. Despite Plaintiff's protests, Swamy told Plaintiff that she would compose a letter to NHLBI for the termination and would share the letter with Plaintiff prior to submitting it to the NIH system, which Swamy did not do.

95. Defendant Rynn's termination of Plaintiff's new R01 negatively impacted the professional career of Plaintiff and several of her colleagues. It negatively impacted Plaintiff's professional reputation, and significantly Plaintiff's financial support, given that 30-50% of Plaintiff's university salary would have been covered for at least five years by this grant.

96. Despite being told that Defendant Rynn had terminated her grant, Plaintiff continued to receive messages from the NHLBI concerning her need to complete activities consistent with the grant being active. To address these emails, on April 19, 2019, Plaintiff wrote to Dr. Swamy, who had indicated previously on January 23, 2019, that she would provide Plaintiff Jiang with correspondence to NIH regarding the termination of the grant.

> Dear Dr. Swamy,
>
> May you please verify the relinquishment of my new R01(R01 HL140060) for us? I have not seen the letter or report to NIH that you said you would share with me during our meeting on 01/23/19. Dr. Compton, the Psychiatry department CRU director, has verbally informed me that the termination of the R01 has been formal. However, I continue receiving notifications from NHLBI regarding activities that I, the PI of the project, need to address, and reminder that I am late in responding to those requirements. I did not respond because I have been following the guidance of our CRU that we not communicate with NHLBI regarding this matter. I view having a formal notification of the R01 relinquishment is necessary for our record keeping.
> Best, Jan

97. Significantly, Dr. Swamy replied on April 25, 2019:

> Jan,
>
> Thank you for your email and my apologies in not responding to you sooner. Please see the attached documentation that Duke has relinquished the grant. As we discussed previously and is stated in the Duke Faculty Handbook (appendix P, page 41), faculty are not

> permitted to communicate with external sponsors on administrative issues. We also discussed that you would like to speak with your program officer, Catherine Stoney, about your continued interest in the research from a scientific perspective. You may do that but only with someone from your department/CRU leadership or School of Medicine Leadership included on the phone call with you. I have copied Scott and Moira on this email so that you may work with them to determine next steps and who to include on such a call if you would like to proceed with that plan.
>
> Thanks, Geeta

98. This email provided Plaintiff with no documentation regarding Defendant Rynn's cancellation of her grant, and also with further evidence of Defendant Rynn's attempts, through Dr. Swamy, to continue Defendant Rynn's efforts to insulate Plaintiff Jiang from having any contact with anyone who could question or oppose Defendant Rynn's discriminatory and retaliatory treatment of Plaintiff Jiang.

99. Eventually Plaintiff learned that Michael Dickman had sent an email to Christina Rinaldi at the NIH/NHLBI on March 6, 2019, stating that the University wanted to "initiate the process" for relinquishing the first-year budget award of $799,690.00 to the U.S. Department of Health and Human Services, Public Health Service 1R01-HL140060-01A1.

100. Also, not content to sabotage her research career in the United States,

Defendant Rynn then informed Plaintiff that she would not be allowed to take her April trip to China due to the need for her to stay at Duke in case she needed to address issues emerging from the audits. In addition, Rynn also denied Jiang's request that her salary be supplemented by a group with which she had been collaborating in China without giving her a reason.

101. On January 30, 2019, the IRB had issued a "Notice of Review of Safety Event" and stated that upon review of the CRU report and presumably Plaintiff's response, the IRB "declared that the problem/event does not represent an Unanticipated Problem Involving Risk to Subject or Others (UPIRTSO). No further action is required."

102. On February 22, 2019, Plaintiff wrote an email to Defendant Rynn imploring her to reconsider forbidding Plaintiff to travel to China in which she stated:

> I established my academic commitment to China in 2003. I have set up two primary goals to achieve in China this year, one is to enhance the understanding and resolving the fear and fear related symptoms emerging from significant physical events, and the other is to make the team approach in health provision more comprehensive and accepted inmedical practice in China. You may find the topic of my formal talk in the April international CV conference (Formal invitation attached) of interest. I have also attached for you a brief description of why

> implementing mental health and integrated care is particularly important.
>
> To accommodate your requirements, I am willing to reduce my trip to nomore than 10 work-days and have also taken an extra week of inpatientservice in April 2019. I highly appreciate your re-consideration and approval of my trip to China, so I can have an uninterrupted academic practice there.

103. Defendant Rynn then scheduled a meeting with Plaintiff to discuss a "clinical matter" and also "to review your academic and clinical financial support."

104. Plaintiff was concerned and asked the Faculty Ombudsman to attend the meeting, Dr. Tom Metzloff. At first Rynn refused to let him attend. Eventually, after discussion of the clinical matter, she then permitted him to come into the meeting.

105. The remainder of the meeting, about 40 minutes, involved Defendant Rynn reiterating that for Plaintiff's sake, she could not allow Plaintiff to leave Duke Campus because Plaintiff might need to respond to questions about the REMIT study. During the meeting, Defendant Rynn became more and more restless and irritable when both Dr. Metzloff and Plaintiff offered that the department CRU director Scott Compton had indicated that Plaintiff could respond via electronic communication. At one point, Defendant Rynn accused

Plaintiff of being too calm, and stated that if she were Plaintiff, she would be anxiously staying at Duke, not going anywhere else.

106. After the meeting, Dr. Metzloff offered to Plaintiff that it might ease the obviously hostile behavior of Defendant Rynn towards Plaintiff if Plaintiff were to agree not to go to China. Plaintiff reluctantly agreed.

107. In fact, during the time period Plaintiff would have been in China, there were no face-to-face interactions required about any matter related to the REMIT study.

108. Dr. Blumenthal and other physicians in the psychiatry department had never heard of a physician/researcher being denied time to undertake professional outreach in other countries and could not understand the source of the hostility of Dr. Rynn towards Plaintiff.

109. Undaunted by the IRB's lack of concern with the exclusion criteria applied in the REMIT study and determined to destroy Plaintiff's research and career, and unsatisfied with having cancelled her outreach trip to China, Defendant Rynn. upon information and belief, either made or caused to be, made an accusation of research misconduct involved the REMIT study to the U.S. Department of Health and Human Services (US DHHS) Office of Research

Integrity (ORI).

110. As a result of the accusation, on March 4, 2019, the US DHHS ORI Research Integrity Officer (RIOO) then requested that Defendants "conduct an inquiry into allegations of possible falsification of the REMIT clinical research records. The purpose of the inquiry would be to determine if there were evidence of potential research misconduct that would warrant an investigation. The inquiry will be conducted by members of our Standing Committee on Misconduct in Research (SCMR)." Plaintiff learned of this next step from Donna Kessler on March 11, 2019, when she was informed that the US DHHS requested inquiry into "research misconduct" would be referred to the university's Standing Committee on Misconduct in Research (SCMR).

111. Plaintiff's FOIA request to the NIH for information related to this inquiry has been outstanding despite repeated requests for over two years.

112. Unbeknownst to Plaintiff at the time, and despite her inquiries about her grant, on March 6, 2019, an email was sent from Michael Dickman with the Duke Office of Research Administration to Christina Rinaldi, National Institute of Health (NIH) representing that Duke University wished to relinquish the funds associated with the new five-year grant awarded to

Plaintiff Jiang. On that same date, the remaining funds for the first year of the public health service research grant terminated by Defendant Rynn ($799,690.00) were returned to US DHHS, Public Health Service.

113. Rynn continued to prohibit Plaintiff from moving forward with her co-investigators to obtain the "independent" and "expert" opinion requested by the IRB in December 2018.

114. On March 25, 2019, Duke University announced a substantial payment to the United States to settle a case involving research misconduct involving falsification and fabrication of data in research funded by the NIH and EPA.[2]

115. The SCMR interviewed Dr. Stephen Boyle, Plaintiff Jiang's co-author on the REMIT study publications, on May 21, 2019. Plaintiff Jiang was interviewed by the Committee on June 17, 2019. On July 15, 2019, the SCMR interviewed Jennifer Wilson, who had served as one of the REMIT Study coordinators, of which there were several, including Pamela Bonner.

116. On March 25, 2019, the SCMR initiated a re-evaluation (re-reads) of echocardiograms from the REMIT study by Dr. Pam Douglas with the Duke Clinical Research Institute.

[2] https://today.duke.edu/2019/03/message-duke-community-about-research-misconduct-case

117. Dr. Douglas was not as experienced as the cardiologists on the REMIT study who originally read the echocardiograms involved. Nor was she an "expert" and independent opinions that the IRB had recommended by obtained.

118. Studies funded by the NIH have found that "[t]he diagnostic accuracy of novice [transthoracic echocardiogram] TTE interpretation is known to be low . . . ."[3]

119. In addition, on April 11, 2019, the SCMR initiated a statistical re-analysis of the primary REMIT study outcomes provided in the 2013 JAMA publication of the study results.

120. Previously, Defendant Rynn had commissioned Susanna Stevens and Lilin She to evaluate the REMIT date conclusions in the JAMA article published by Plaintiff and her co-investigators. In an email on March 8, 2019, she stated the following:

> As the first step, Susanna and I have tried to replicate a few key numbers for the primary results published in JAMA using the same patient population and the same datasets and programs sent to DCRI. We can replicate some of the numbers but cannot replicate some others. Overall, our numbers are very close to what were published. If we have more time, we would like to investigate

[3] Journal of Echocardiography, J Echocardiogr. 2021; 19(4): 222–231. (Published online 2021 May 29. doi: 10.1007/s12574-021-00531-y https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8556165/)

> further on why we could not match 100% with the JAMA paper.
>
> As the second step, we also re-ran the SAS programs after excluding those 26 subjects who are considered as not eligible according to the recent assessment. The results are slightly changed. You can review the differences in the attached tables. Since we now have a smaller sample size, the p-values are changed. However, the results obtained from this reduced patient sample are in general very similar to the results published in JAMA.

121. This email was not shared with Plaintiff at the time, and she only learned of it later and not from Defendant Rynn.

122. After Plaintiff learned that the SCMR had initiated in April 2019 a re-evaluation of the echocardiograms conducted during the study between 2006 and 2015 by Pam Douglas and the apparent presumption that there were "ineligible subjects," she scheduled a meeting with Paul Lantos, Jody Power, and Walter Lee, members of the Duke IRB, to discuss Plaintiff Jiang's concerns regarding the SCMR's draft conclusions.

123. Plaintiff expressed her concern about the potential determination that there were "ineligible subjects" and fact that re-calculations were being done of the statistical analysis using numbers different from those used by the investigators who conducted the study.

124. In addition, Plaintiff also expressed her concern about the analysis of the

echocardiograms re-read by Pam Douglas, M.D. because she did not have the same training as the cardiologists who served as co-investigators with Plaintiff.

125. At the meeting, Jody Power, Duke IRB Chair, denied making any comment about needing to "dive deeper" (in REMIT) to Scott Compton or anyone.

126. Plaintiff Jiang sent a follow up email after the September 12, 2019, meeting on September 30, thanking them for meeting and inquiring about the IRB review and consideration of the SCMR inquiry. Dr. Lantos responded on October 6 and confirmed understanding of Plaintiff Jiang's concerns about the application of principles recently developed to work done during the REMIT study. Significantly, he assured Plaintiff Jiang that they would not "reevaluate 2006 science using 2019 eyes."

> Hi Jan,
>
> > Thanks again for coming over to meet us. We certainly heard and acknowledge your concern about whether a reevaluation of the echo data from the REMIT study might cast doubt on your findings primarily dueto advances in echocardiography in the years since REMIT was done.
> >
> > We hopefully provided some reassurance that this would be an unlikely outcome, as our goal is not to reevaluate 2006 science

> using 2019 eyes. There is really a spectrum of outcomes, with the extremes being that an audit fully confirms the original findings or it's completely incompatible with them. In between these two there could certainly be a gray area in which the original findings would be seen asreasonable. If it happens that the audit finds major fault with the original findings, I can't imagine that this would lead to a summary judgment or action without first diving deeper into these findings, and certainly making sure you and your collaborators aware.
>
> I believe that was the understanding we reached during the meeting.Please let me know if there is anything you believe I missed.

127. Plaintiff Jiang wrote back and thanked him and expressed encouragement. She also expressed that the audit had been ongoing for over a year and that she had been forbidden to publish manuscripts or doing research and she had been prevented from sharing her thoughts and concerns about the audit.

> Dear Paul,
>
> Thank you very much for your message summarizing the key element we discussed during our meeting. I am particularly impressed by your comment that "our goal is not to reevaluate 2006 science using 2019 eyes". My perception for the "Our" is that it means Duke IRB. Please clarify if my perception is wrong.
> I am much encouraged and confident now regarding the continued REMIT audit that has been happening for more than a year and remains being open ended. With it, I have been forbidden to publish several manuscripts produced from the REMIT biomarker study and been forbidden from doing research as PI. I have not

> given any permission to share my thoughts/concerns for certain issues in the REMIT audit.
>
> I would like to ask you all to provide me update, if possible, on what further evaluation you are doing before I receive the final conclusion of the REMIT audit.
>
> Sincerely,
>
> Best, Jan

128. On October 22, 2019, the SCMR issued a report concluding that no research misconduct had occurred. Despite finding **no research misconduct occurred,** the SCMR exceeded its charge to investigate this allegation: "Possible falsification of the clinical research record for the Responses of Myocardial Ischemia to Escitalopram Treatment (REMIT) clinical research study."

129. Instead the SCRM report contained opinions regarding "protocol deviations." In fact, the REMIT study had IRB approved protocols for every year in which patients were enrolled. Nonetheless, the SCMR determined that protocol deviations had occurred and made several recommendations again, wholly outside the scope of their authority.

130. While the SCMR was investigating research misconduct, on July 12, 2019, Plaintiff learned about a School of Medicine/Duke Health position for

Assistant Director positions to work with the new Center for Interprofessional Education and Care which was created to expand opportunities for learners and clinicians throughout the health system to enhance their skills in interprofessional practice, working with the Center Director Mitch Heflin (Dr. Heflin), and focusing on the areas of preclinical and clinical education, faculty development, evaluation and scholarship. The announcement also indicated that applications required a cover letter summarizing interest, a copy of the applicant's curriculum vitae, and most significantly for Plaintiff, a letter of support from the applicant's department chair, division, or program head, attesting to the applicant's qualifications and their support for the applicant's time, which was estimated to be one day a week.

131. Plaintiff Jiang reached out on July 15, 2019, to Jeannie Beckham and Defendant Rynn regarding Plaintiff Jiang's interest in the position and asking for their support for her application.

132. Plaintiff Jiang also reached out on July 16, 2019, by email to Dr. Heflin, the Center Director and contact for the position, and expressed her interest and asked whether there were funds available to cover the time spent in the position because her chief wanted to know. Dr. Heflin replied that there were

funds available.

133. Defendant Rynn did not respond to Plaintiff Jiang's email until July 23, at which point she indicated that she wanted to set up a meeting to discuss the matter of Plaintiff Jiang's application. Plaintiff Jiang met with Defendant Rynn and Jean Beckham, and they declined to support her application for the position.

134. On July 31, 2019, Plaintiff Jiang wrote an email to Defendant Rynn to summarize the discussions at the meeting which included both Plaintiff Jiang's proposed Fall trip to China and the School of Medicine position:

Dear Moira,

Thank you for taking time to meet me.

> I would like to summarize what I have learned from you at the meeting.
>
> 1. Re: My application request to response to the call of the Duke IPEC
>
> I heard from you that you have reached out to the Duke IPEC and learned that the program is looking for individuals who have had a high volume of outpatient services. Such individual will be in leadership of leading IP outpatient service. You have discussed with Dr. Shirey (may be others that I could not recall names) and made your nominations to IPEC. You will not make any new nominations for the AD position of the Duke IPEC. It is your opinion that I am not at the level of the IPEC is looking for.

2. My visit to my mother in China in the fall

You gave me your support for it, provided that I work out with Dr. Holmer for not having conflict on inpatient service.

Best, Jan

135. Rynn then responded to Plaintiff Jiang's email:

Yes, reached out to SOM and Drs. Holmer and Heilbron for appropriate nominations who stressed the importance of leadership experience of a multi-discipline professional team and strong communication skills.

And if we could please have your vacation dates that you plan to take. Thanks, Moira

136. Because Defendant Rynn refused to support Plaintiff Jiang's application for the position, Plaintiff Jiang then reached out to Dr. Heflin to communicate Defendant Rynn's decision not to support Plaintiff Jiang's application.

Defendant Rynn informed me that she has reached out to SOM and Drs. Holmer (Psychiatry inpatient service director) and Heilbron (Psychiatry department vice Chair for clinics) for appropriate nominations who stressed the importance of leadership experience of a multi-discipline professional team and strong communication skills. Dr. Rynn learned that your IPEC program is looking for individuals who have had a high volume of outpatient services. Such individual will be in leadership of leading IP outpatient service. Dr. Rynn has made her nominations to IPEC and will not make any new nominations for the AD position of the Duke IPEC. Dr. Rynn thinks I am not at the level of the IPEC is looking for.

Best, Jan

137. Dr. Heflin replied that Dr. Rynn was mistaken that there was a preference for individuals with a high volume of outpatient services and that he would be happy to answer any questions for Dr. Rynn. Plaintiff Jiang considered whether it would be worthwhile for Dr. Heflin to reach out to Defendant Rynn but decided against doing so as it was clear to Plaintiff Jiang that Defendant Rynn would not support her no matter. Feeling discouraged and victimized by Defendant Rynn's bullying over the months since the audit commenced and Defendant Rynn unilaterally cancelled her five-year grant, Plaintiff Jiang engaged in introspection about the matter and determined to pose a direct inquiry to Defendant Rynn about Plaintiff Jiang's status at Duke.

138. In October, another opportunity involving executive leadership in academic medicine (ELAM) became posted and once again Plaintiff Jiang discussed with her chair, Defendant Rynn, and sought her support per the job announcement. In a curt, one sentence response, Defendant Rynn replied: At this point in time, I am unable to support your application for this program. Dr Jiang sought an explanation: "That's disappointing. I'd highly appreciate if you may provide me the reason(s) underlying your decision. Jan" the same

day and again, Defendant Rynn's reply was curt and lacked any substantive information: "It is based upon the issues we have already discussed."

139. On August 2, 2019, Plaintiff wrote Defendant Rynn an email stating:

> Dear Moira,
>
> In thinking about our recent conversations, it appears that my role as a tenured, full Professor in our Department has changed significantly over the past year. I need you to clarify your position regarding several recurring issues that we have discussed over the past several months:
>
> 1. My research activities: It is my understanding that you have forbid[den] me from conducting any research in which I am a principal investigator. This restriction includes my examining data from previous studies, writing manuscripts, and applying for new funding from the NIH, industry, or other funding sources. Am I correct that this is your position, and if it is, when can I expect this restriction to be lifted?
>
> 2. My international collaborations: It is my understanding that you are not permitting me to pursue my ongoing collaborations with my longtime Chinese colleagues, including not allowing me to travel to China or developing a formal contract with academic centers in China. If this is correct, please provide me with an explanation for your position and an indication of under what circumstances will this restriction be lifted.
>
> 3. My professional activities: It is my understanding that you want to limit my professional activities to the inpatient service and to supervise and train residents and medical students on the inpatient service. Is this correct?

4. My new R-01 grant that's relinquished: It was my understanding at the meeting with you and Dr. Swamy that Dr. Swamy planned to compose a letter to NHLBI with reason(s) for the relinquishment. She would share the letter with me prior to communicate with NHLBI for the action. You did not think that was what Dr. Swamy meant.

To make sure there is no misunderstanding, I would appreciate your confirming that this is how you have defined my role in the Department at this time and what I can expect going forward. Thank you for taking the time to respond to my request.

Sincerely, Wei Jiang

140. On August 9, 2019, Defendant Rynn responded:

Dear Jan,

Thank you for your most recent email, although I will say that I was surprised to again see questions listed that we have provided answers to in multiple previous communications.

To summarize, the research audit that remains underway regarding your studies is a serious matter and we appreciate your attention and full participation with of our colleagues in the School of Medicine who are working on our behalf to understand and guide us through the next steps. At this time, as the audits are underway, I am putting your approved research activities on hold, to include the submission of new awards. The findings to date clearly outline the need for additional training and resources to enable you to begin to work in research at the highest level of integrity and quality. As a senior faculty member and PI, I expect you to understand and recognize the importance of this support that the Department is providing to you at this time. I also remind you that the NIH and other federal agencies hold Duke – as well as the PI – responsible for adherence to quality.

The expectations for a senior level hospitalist provider are clear and consistent across our PDC provider group. I do understand you are scheduled to work and support patient care services across Duke Health inpatient services this fiscal year. In addition, again consistent with our training programs within the Department of Psychiatry, providers are expected and encouraged to work/teach trainees of all levels in their specific work setting.

Lastly Jan, I do understand that this has been a terribly stressful time and I will again share that the senior leadership team for Research and the Chair's office, along with our partners across the School of Medicine, are working in your long-term interest as we take the necessary steps to demonstrate your ability to conduct quality research.

I do not at this time approve professional requests for extended travel that takes you from our clinical operational needs here at Duke, as well as the audit process related to your research program.

All faculty have the same access to vacation and extended leave requests in accordance with the faculty handbook, https://provost.duke.edu/sites/all/files/FHB.pdf. According to the handbook, faculty with twelve-month appointments in the Medical Center have compensation that covers eleven months of effort and one month of paid vacation. One month of paid vacation is equal to 22 business days and PDC vacation policy. Please review these resources to determine any further leave at this time. Division Director approval is required for any extended leave related to FMLA etc.

Thanks again Jan for your continued participation in the research inquiry and follow-up. We appreciate all that you do to support our patients and trainees across our inpatient services. We will continue to be in touch regarding feedback on research review.

Moira

141. Dr. Blumenthal and other members of the psychiatry department had never seen a researcher and full professor prohibited from being prohibited from doing research either in her own laboratory or in other laboratories. At this time, due to Rynn's refusal to let Plaintiff be involved in any research work even though no patient safety concerns had ever been identified, Plaintiff was reduced to providing only clinical services, which was unheard of.

142. In fact, Rynn sent word to Blumenthal through his staff that Plaintiff was not to be paid for any work on his grants. Blumenthal refused to suspend payments to Jiang. Rynn then directed Blumenthal to keep Jiang away from working with any data.

143. Prior to the release of the final report, and when it became aware that the IRB was going to consider the SCMR report, Plaintiff contacted Donna Kessler on October 16, 2019, and expressed concern that "independent and expert" evaluations had not been obtained as requested by the IRB. Plaintiff also expressed concerns she, Plaintiff Jiang, as the principal investigator, and her co-investigators, Dr. O'Connor, Dr. Velazquez, and Dr. Samad, had not been allowed to obtain "independent expert opinion on these issues and report

back to the Board with their conclusion." Finally, Plaintiff expressed concerns that she and her co- investigators were completely cut out of the process of obtaining independent and expert options and that Dr. Douglas was selected presumably by Defendant Rynn or others at her behest to do the analysis.

144. Plaintiff also told Kessler that the two -cardiologists who analyzed the REMIT echo images originally had been trained on how to analyze REMIT echo images. In addition, they analyzed all the images consensually whereas Dr. Douglas only re-read a proportion of REMIT echo images for unclear reasons and there is no indication that she read the images in consultation with any colleagues, and certainly not with any colleagues trained in this area. Finally, Dr. Douglas provided no explanation as to how she produced the EF scores she included in her evaluation. In fact, the echo-cardiology lab which did the original reading used software to analyze the REMIT echo images and produce the original EF scores and the REMIT cardiologists validated these measurements.

145. As for the actual design of the study which Dr. Douglas criticized, in fact, the REMIT study was designed between 2003 and 2006 and used the best methods at that time relating to when and how the echocardiogram should be

utilized in mental stress and exercise stress testing. Dr. Douglas' evaluation in March 2019 imposed her opinion of 2019 design standards on a study designed more than ten years prior.

146. Finally, Dr. Douglas failed to perform a thorough evaluation on the REMIT echo images in that she did not re-read for the eligible participants both baseline and endpoint mental stress echocardiograms for the same participants. Instead, she only re-read a randomized sample of individuals with baseline results and a different randomized sample of individuals with endpoint results. Despite Dr. Douglas' failure to re-read consistently both of baseline and endpoint echocardiograms for a randomized group of participants who had both baseline and endpoint echocardiograms, she provided a statistical analysis to support her conclusions in paragraph 9 regarding percentages of "agreement" with the original REMIT study findings concerning both baseline and endpoint assessments.

147. O'Connor, Velazquez, and Samad had reviewed the re-evaluation of the echocardiograms and concluded that they were flawed, and Plaintiff Jiang also raised this issue with Donna Kessler as well, prior to the release date of the report on October 22, 2019.

148. Nonetheless, on October 22, 2019, the Duke Standing Committee on Research Misconduct (SCRM) was issued and concluded that there was no evidence of falsification or fabrication ofstudy records. The report again noted that the beta blocker and exercise stress testing amendments form the original protocol and again alleged they were not communicated to the IRB as required. But significantly, no new information was provided by the SCRM inquiry.

149. Despite having concluded that there was no research misconduct, which should have been the end of the inquiry of the SCMR, the SCMR nonetheless recommended:

> 1. The managing editors of the 2012 Am. Heart J. (Jiang et al.) and 2013 JAMA (Jiang et al.) publications should be contacted with the known information about the reporting of the REMIT study conduct and results to determine if corrections and/or retractions may be needed.
>
> 2. The Department/CRU, along with Plaintiff Jiang and the applicable co- authors, should review the other REMIT study publications to determine whether the research is accurately represented in those publications or if the managing editors of the journals should be contacted about possible corrections or retractions.
>
> 3. Plaintiff Jiang should attend a robust workshop on Good Clinical Practice and the requirements of clinical research equivalent to what would be needed to obtain certification as a Certified Principal Investigator or Certified Clinical Research Professional . . .

4. If Plaintiff Jiang will be applying for future federal funding to conduct research, she should attend the Responsible Conduct of Research Short Course conducted by the Trent Center for Bioethics or an equivalent program.

150. Plaintiff Jiang was already scheduled to take personal leave, and not scholarly leave, to visit China to do outreach and visit her family because of Defendant Rynn's refusal to approve scholarly leave (in an email on August 9, 2019). Thus, Plaintiff was in China from October 17 to November 22, 2019, and thus on the date that the final SCMR report was issued.

151. Plaintiff Jiang was offered the opportunity to provide a response to the SCMR report by December 6, 2019, but given her trip and her other work expectations, on November 12, 2019, Plaintiff Jiang requested an extension due to her need to carefully consider the report, given that over a year had been spent between the OARC and the SCMR investigations/inquiries, and also due to the fact that while in China, Plaintiff Jiang was having to care for her 87-year old mother who had become critically ill.

152. On November 13, 2019, Donna Kessler, Duke Research Integrity Officer, replied to Plaintiff Jiang's request for an extension and denied it, stating that the University's response from the Dean Mary Klotman was due to the US

DHHS Office of Research Integrity (ORI) by December 5th. Dr. Kessler did not apparently consider whether the University could or should request an extension of time due to Plaintiff Jiang's request. Kessler then reiterated Plaintiff Jiang's deadline of November 18 to get her comments to Dr. Klotman for a final submission on December 5, 2019.

153. On November 15, 2019, Plaintiff Jiang then reiterated an earlier question that she had made regarding the Echo re-read matter previously raised and included in the SCRM report and again questioned the source of the allegations made to the US DHHS / NIH Research Integrity Office about research misconduct. On the same day, Kessler replied but did not identify the source of the allegations made about research misconduct.

154. As a result of the SCMR report and the false conclusions about noncompliance with IRB approved protocols, Defendant Klotman then wrote Plaintiff on November 22, 2019, prior to responding to the US DHHS regarding the allegations of research misconduct. In her letter Defendant Klotman agreed with the SCMR conclusion that confirmed insufficient evidence of research misconduct and agree with the additional corrective actions recommended by the SCMR. Dean Klotman stated she would consider Plaintiff

Jiang's response to the SCMR report to be provided by December 5, 2019.

155. On November 26, Plaintiff Jiang conferred with the Duke IRB chair Paul Lantos and also with Ombudsman Thomas Metzloff regarding Plaintiff Jiang's desire to consult with the original REMIT cardiology co-investigators / collaborators who provided the original cardiology and statistical analysis for the original study due to their expertise in echocardiography. Dr. Lantos emailed her and indicated that he "wanted to confirm, having spoken with Jody, that the IRB would like the cardiologists who were on your study to have the opportunity to review and respond to the echo audit, even if they are no longer at Duke." Plaintiff Jiang had explained that Defendant Rynn had previously instructed her NOT to reach out to the original team who worked on the study because they were no longer at Duke. In fact, when Plaintiff had raised the issue with the IRB about Defendant Rynn's forbidding her to contact her co-investigators about the re-evaluation of the REMIT study, Paul Lantos had responded as follows:

> My personal point of view is you did your science as a team and it should be the team that responds to an audit or investigation, especially for something like echo interpretation or statistics for which you have coinvestigators who are experts.
>
> I do not think we as the IRB have any authority to tell you whom

> you can or can't consult with, nor do we have the authority to override instructions from others to NOT speak with anyone.
> Tom will be able to answer this better than I, but I'm not sure you can really be prohibited from speaking with someone unless it's on the advice of Duke counsel or it's a case of protected information that can't be shared. It's worth contesting any instructions you've gotten to not speak with your collaborators if you feel they are unfair or against policy.

156. On December 12, 2019, the Duke IRB was provided a copy of the OARC report and reviewed the same on December 19, 2019, to determine whether the event represented an Unanticipated Problem Involving Risk to Subjects or Others (UPIRTSO). Having concluded it did not, on December 26, the Duke IRB issued a notice of review stating that no UPIRTSO had occurred and that further reiterating that the "PI and Investigators, with the support of the CRU and School of Medicine, should seek independent expert opinion on these issues and report back to the Board with their conclusions."

157. Notwithstanding the Dean's recommendations that the SCMR recommendations be implemented, in January 2020, Defendant Rynn then imposed draconian sanctions which had the effect of ending Plaintiff's research career completely.

158. Again, Dr. Blumenthal and other physicians in the Department had never seen such disproportionate sanctions applied and over a difference of

opinion about the inclusion/exclusion of subjects in a study and protocols amended due to safety reasons. While other members of the department had noticed that Rynn had targeted other non-White, (of Asian and Indian descent) older male department members, they also noted that she had never gone after anyone to the extent as Plaintiff.

159. On January 29, 2020, Defendant Rynn admitted to Plaintiff Jiang that she had instigated all of the reviews and audits even though she never believed that Plaintiff or her co-investigators had engaged in any research misconduct.

160. At this same meeting, Plaintiff Jiang then informed Defendant Rynn that she had a research support fund of $48,847.00 with the Behavioral Medicine Research Center (BMRC). Defendant Rynn then informed Plaintiff Jiang that she could not use that money for her salary support.

161. Dr. Blumenthal and others in the department had never observed other physicians, included white male physicians / researchers, be subjected to such treatment.

162. Although the BMRC had previously been led by Dr. Redford Williams, Plaintiff Jiang was aware that Defendant Rynn had removed Dr. Williams from the directorship sometime in middle of 2019 and had herself has been

serving the interim director of the BMRC since doing so.

163. Furthermore, Plaintiff Jiang had a $20,805.40 fund for mental health outreach in her own discretionary account, but since March 2019, Defendant Rynn had forbidden Plaintiff Jiang to leave the Duke campus for any academic activities, such that this money was also unavailable to her.

164. Despite having reduced Plaintiff's salary to less than $50,000, and restricted her to solely clinical duties, in December 2019, Rynn offered a salary of $220,000/year to a non-Asian younger physician with 90% clinical duties comparable to the duties being performed by Plaintiff at that time.

165. During Rynn's tenure as Dean, she also instigated audits and investigations of two other physicians from India who eventually left employment with Defendants after Rynn's hostile treatment which was excessive in comparison to treatment of similarly situated younger, white colleagues.

166. In April 2020, Plaintiff appealed to Defendant Klotman who informed Plaintiff on May 29, 2020, that she supported

> the decision of Defendant Rynn to implement more restrictive corrective actions based on the totality of information available to her regarding your work within the Department. The corrective actions you outline from my November 22, 2019 letter to Donna

> Kessler are based solely on the recommendations provided by the Standing Committee on Misconduct in Research. The corrective actions outlined in my November 22, 2019 letter do not take into account other audits, reviews, or information known to the Department at the time Dr. Rynn made her decision.

167. Despite inquiry by Plaintiff, neither Defendant Klotman nor Defendant Rynn never identified the additional "totality of the information" nor "other audits, reviews, or information known to the Department" at the time Defendant Rynn imposed her more severe sanctions.

168. On November 12, 2020, and then on November 20, 2020, when she filed her charge of discrimination, Plaintiff complained about the discriminatory treatment to which Rynn had subjected her.

169. On December 18, 2020, Defendants retaliated against Plaintiff by writing to the editor of JAMA calling into question the legitimacy of the article regarding the REMIT study. **Exhibit 4, pp 1-3.**

170. The only corrections noted for the JAMA article were typographical in nature. **Exhibit 2, pp 1-2.**

171. Plaintiff wrote a letter to the editor of JAMA accepting the need for technical corrections and providing a response to Compton's allegations about the inclusion/exclusion criteria. **Exhibit 2, pp 4-6.**

172. On December 22, 2020, Compton wrote Plaintiff's co-investigators about the JAMA article. **Exhibit 2, pp 8-10.**

173. On January 21, 2021, on behalf of the co-investigators, Chris O'Connor wrote JAMA questioning the internal methodology used to evaluate the REMIT study, and raising numerous other issues regarding the Defendants' evaluation of the REMIT study. **Exhibit 2, pp 11-15.**

174. On March 18, 2022, Geeta K. Swamy, M.D. wrote to JAMA again and made allegations that the study did not comply with the protocol initially approved by the IRB. **Exhibit 2, pp 15-16.** Swamy omitted any mention that the amendment of the protocol was due to safety issues which was specifically allowed by law. She also alleged that there were statistical issues with the data analysis even though the data analysis was based on "intention-to-treat" which does not require evaluation of patient compliance/adherence to inclusion/exclusion criterion after randomization. This allegation demonstrated a fundamental misunderstanding of the intention to treat analysis. Swamy also has much less experience as a researcher than Plaintiff and has a much thinner publication record.

175. JAMA requested Plaintiff respond to Defendants' latest attack on the

JAMA article authored by Plaintiff and her co-investigators. On April 18, 2021, Plaintiff updated JAMA on her forthcoming response to Defendants' correspondence regarding the JAMA article. **Exhibit 2, pp 17-18.**

176. On April 19, 2021, Plaintiff provided a fulsome response to Defendants' continued misguided, malicious, discriminatory and retaliatory attacks on the JAMA article. **Exhibit 2, pp 19-26.**

177. Since September 12, 2022, Plaintiff has been in China on leave taking care of her mother and has requested Sabbatical leave, to which she is entitled as a tenured faculty member. Defendants have refused to provide her any response to her repeated requests made on at least four occasions, with the last one being March 4, 2023. Moreover, Plaintiff's husband was recently informed that Defendants had providing information to government authorities indicating the Plaintiff had "retired" which she clearly has not. This action is again indicative of Defendants' discriminatory treatment of Plaintiff based on her age.

COUNT ONE: TITLE VII AND ADEA
RACE, COLOR, AGE, AND SEX
DISCRIMINATION AND RETALIATION
IN VIOLATION AGAINST DEFENDANTS DUKE AND DUHS

15. Plaintiff is female, of the Chinese race and ethnicity, and older than 40

(over 70).

16. Defendant Rynn is much younger than Plaintiff.

17. Plaintiff is a member of several protected classes (older, non-White, Asian, and female) and was qualified for her position when she was subjected to a hostile work environment and discriminated against and retaliated against due to her membership in these protected classes.

18. Defendants took multiple adverse actions against Plaintiff due to discrimination based on her age, sex, race, and ethnicity.

19. Defendants took multiple adverse actions against Plaintiff due to her opposition to illegal discrimination.

20. Defendants treated other non-white (Asian and Indian descent) department members more favorably than Plaintiff.

21. Defendants treated other male department members more favorably than Plaintiff.

22. Defendants treated other younger department members more favorably than Plaintiff.

23. Defendants treated other department members who did not complain about illegal discrimination more favorably than Plaintiff. When Plaintiff

complained about discrimination, Defendants took additional adverse actions against Plaintiff due to her protected activity.

24. Plaintiff has suffered damages as a result of Defendant's unlawful discriminatory and retaliatory actions, including emotional distress, past and future lost wages and benefits, and the costs of bringing this action.

25. Defendant intentionally violated Plaintiff's rights under Title VII and the ADEA, with malice or reckless indifference, and, as a result, is liable for punitive damages.

COUNT TWO: RACE DISCRIMINATION AND RETALIATION SECTIONS 1981 AGAINST DEFENDANT RYNN AND DEFENDANT

26. Plaintiff Jiang's race and national origin is not white / Caucasian (Asian).

27. Defendants treated other non-white / Caucasian (non-Asian and non-Indian descent) employees more favorably.

28. Defendants took multiple adverse actions against Plaintiff due to her opposition to illegal discrimination.

29. Plaintiff suffered damages due to Defendants unlawful discriminatory and retaliatory actions, including emotional distress, past and future lost wages and benefits, and the costs of bringing this action.

30. Defendant intentionally violated Plaintiff's rights under section 1981

with malice or reckless indifference, and, as a result, is liable for punitive damages.

PRAYER FOR RELIEF

WHEREFORE, the Plaintiff respectfully prays that this Court:

1. Issue an injunction directing the Defendants to restore Plaintiff's previous status;

2. That this Court enjoin the Defendants from discriminating on the basis on race, color, sex and age in the terms and conditions of employment and from engaging in retaliatory actions when dealing with individuals who complain about illegal discrimination;

3. That this Court order Defendants to make whole Plaintiff by providing her with appropriate lost earnings and other lost benefits, with prejudgment interest, in amounts to be proved at trial, and other affirmative relief necessary to eradicate the effects of its unlawful employment practices, including, but not limited to, reinstatement to her previous salary and restoration of the amounts she has lost in research funding as a result of Defendants' actions;

4. That this Court order Defendants to make whole Plaintiff by providing compensation for nonpecuniary losses, including emotional pain, suffering,

inconvenience, and mental anguish in amounts to be proven at trial;

5. That this Court order Defendants to institute and carry out policies, practices, and programs which provide equal opportunities to qualified individuals, and which eradicate the effects of past and present unlawful practices, including discrimination and retaliation;

6. That this Court award the Plaintiff reasonable attorney's fees and the other costs of this action;

7. That this Court award Plaintiff such other and further relief as may be just and equitable.

JURY TRIAL DEMANDED

Plaintiff requests a jury trial on all questions of fact raised by the Complaint.

Respectfully submitted, this the 22nd day of March 2023.

/S/ VALERIE BATEMAN
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New South Law Firm
209 Lloyd St., Ste 350
Carrboro, NC 27510
T: 919-810-3139
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New South Law Firm
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Charlotte, NC 28207
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Attorneys for Plaintiff

CERTIFICATE OF SERVICE

I hereby certify that I electronically filed the foregoing **AMENDED COMPLAINT** using the CM/ECF filing system which will automatically send email notification of such filing to the all counsel of record.

This the 22nd day of March 2023.

/S/ VALERIE L. BATEMAN
Valerie L. Bateman
NEW SOUTH LAW FIRM

SOSID: 0452120
Date Filed: 6/26/2020 9:09:00 AM
Effective: 7/1/2020
Elaine F. Marshall
North Carolina Secretary of State
C2020 164 00066

ARTICLES OF RESTATEMENT OF DUKE UNIVERSITY HEALTH SYSTEM, INC.

The undersigned corporation pursuant to § 55A-10-06 of the General Statutes of North Carolina hereby submits these Articles of Restatement for the purpose of amending its Articles of Incorporation:

1. The name of the corporation is Duke University Health System, Inc. (the "**Corporation**").

2. The Restated Articles of Incorporation are attached hereto as Exhibit A and incorporated herein by reference thereto. The Restated Articles of Incorporation include an amendment to Article IX.B. revising the list of *ex officio* members. The amended Article IX.B. now reads, in its entirety, as follows:

IX.

B. The Board of Directors shall include five (5) *ex officio* members, who shall be the individuals serving as President of Duke University, the Chancellor for Health Affairs of Duke University / President and Chief Executive Officer of the Corporation, the Chair of the Board of Trustees of Duke University, the Dean of the Duke University School of Medicine and the Chair of the Board of the Duke University School of Medicine faculty practice plan. A minimum of eight (8) members of the Board of Directors shall be current or former Duke University Trustees. At least one member of the Board of Directors shall be a Chair of a Clinical Department in the Duke University School of Medicine. The remainder of the members of the Board of Directors shall be individuals selected to serve on the basis of their ability to contribute to the governance of the Corporation.

3. The Corporation has no members and therefore no members' approval was required for the amendment described herein.

4. This amendment was adopted by the Board of Directors of the Corporation on January 17, 2020.

5. The approval of the Board of Trustees of Duke University was required, and was obtained by resolution of that Board of Trustees on January 17, 2020.

6. These Restated Articles of Incorporation were adopted by the Corporation's Board of Directors in the manner prescribed by Chapter 55A of the General Statutes of North Carolina and contain an amendment not requiring member approval since the Corporation has no members.

7. These Articles of Restatement will be effective as of 12:00:00 a.m., Durham, North Carolina time, on July 1, 2020.

IN WITNESS WHEREOF, the undersigned has executed these Articles of Restatement, this the 7th day of May, 2020.

DUKE UNIVERSITY HEALTH SYSTEM, INC.

By: _____
A. Eugene Washington, M.D.
President and Chief Executive Officer

Exhibit A

RESTATED

ARTICLES OF INCORPORATION

OF

DUKE UNIVERSITY HEALTH SYSTEM, INC.

A Nonprofit Corporation

We, the undersigned, natural persons of the age of eighteen years or more, acting as incorporators for the purpose of creating a nonprofit charitable corporation under the laws of the State of North Carolina, as contained in Chapter 55A of the General Statutes of North Carolina, entitled "North Carolina Nonprofit Corporation Act", and the several amendments thereto, do hereby set forth:

I.

The name of the corporation is "DUKE UNIVERSITY HEALTH SYSTEM, INC.", hereinafter referred to as the "Corporation".

II.

The Corporation is a charitable corporation within the meaning of Section 55A-1-40(4) of the General Statutes of North Carolina.

III.

The Corporation shall have no members.

IV.

The purpose for which the Corporation is organized is to operate an integrated academic health system which will provide medical care, hospital care, medical education, and medical research through hospitals, clinical research organizations, affiliated physicians groups, outpatient clinics, managed health care plans, and other appropriate facilities and related entities, and through affiliations and other relationships with other health care and related service providers. The Corporation shall also provide support, financial and otherwise, to the medical and other educational and research activities of Duke University, a North Carolina nonprofit corporation, including without limitation the Duke University Medical School and other entities affiliated with Duke University.

V.

The Corporation is not organized and shall not be operated for pecuniary gain or profit. No part of the property or net earnings of the Corporation shall inure or be payable to or for the benefit of any individual except as reasonable compensation for services actually rendered by such

individual or as reasonable payments and distributions in furtherance of the purposes set forth in Articles IV and VI hereof. It is intended that the Corporation will qualify at all times as an organization exempt from Federal income tax under Sections 501(a) and 501(c)(3) of the Internal Revenue Code of 1986, as amended, or the corresponding provisions of any future United States internal revenue law (referred to in these Articles as the "Code"), that it will qualify as an organization to which deductible contributions may be made pursuant to Sections 170, 642, 2055 and 2522 of the Code, and that it will qualify as other than a private foundation pursuant to Section 509(a)(1) of the Code. Therefore, notwithstanding any other provision in these Articles, the Corporation shall never be authorized to engage in any activity except in furtherance of the purposes for which the Corporation is organized, and the Corporation (i) shall not carry on any activities not permitted to be carried on by a corporation exempt from Federal income tax under Sections 501(a) and 501(c)(3) of the Code, and (ii) shall not carry on any activities not permitted to be carried on by a corporation, contributions to which are deductible under Sections 170, 642, 2055 and 2522 of the Code. The Corporation shall never directly or indirectly participate or intervene in (including the publishing or distributing of statements) any political campaign on behalf of or in opposition to any candidates for public office. No substantial part of the activities of the Corporation shall be devoted to attempting to influence legislation by propaganda or otherwise within the meaning of the prescriptive provisions of the Code, and its expenditures to influence legislation shall not exceed the permissible limits of Sections 501(h) and 4911 of the Code, to the extent applicable, and shall not be of the type or magnitude that would subject the Corporation to tax under Section 4911 or any other provision of the Code. If and to the extent that Section 4942 of the Code is applicable to the Corporation, the Board of Directors of the Corporation shall cause the Corporation to distribute amounts for each taxable year at such time and in such manner as not to become subject to the tax imposed by such Section. Notwithstanding any other provisions of these Articles of Incorporation, if and to the extent that the following provisions of the Code are applicable, the Corporation and its Directors and Officers shall not engage in any act of self-dealing as defined in Section 4941(d) of the Code, shall not retain any excess business holdings as defined in Section 4943(c) of the Code, shall not make any investments in such manner as to subject the Corporation to tax under Section 4944 of the Code, and shall not make any taxable expenditures as defined in Section 4945(d) of the Code.

VI.

A. The Board of Directors of the Corporation shall cause the Corporation to be operated for its proper corporate purposes pursuant to the authority delegated to the Corporation by the Board of Trustees of Duke University as set forth in these Articles and in the Bylaws of the Corporation.

B. The Corporation shall, not less often than annually, deliver to the Board of Trustees of Duke University a report of operations and financial statements for the Corporation for the period concerned and any other information the Board of Trustees may request. The Directors of the Corporation shall confer, at least once during each fiscal year of the Corporation, with the Board of Trustees concerning the operation of the Corporation and its support of Duke University.

C. Duke University shall be deemed to include its successor by merger, consolidation or otherwise. If Duke University or its successor should cease to exist, substantially terminate or abandon it educational operations, change its purposes or operations to the extent that it no

longer fulfills the charitable purposes and objectives expressed in these Articles of Incorporation, or cease to be a qualifying charitable organization (as hereinafter defined), the Board of Directors of the Corporation shall select and designate a substitute organization which is then a qualifying charitable organization, and all powers, rights, and duties to be held or performed hereunder by Duke University or its representatives shall thereafter be held or performed by such successor organization or its representatives.

VII.

Except as otherwise provided in these Articles of Incorporation or in the Bylaws of the Corporation, the Corporation shall have all of the powers conferred upon nonprofit corporations under the North Carolina Nonprofit Corporation Act.

VIII.

In the event of the dissolution of the Corporation, to the extent allowed under applicable law, all of the assets of the Corporation shall be distributed to, or its assets shall be sold and the proceeds distributed to, Duke University, or if Duke University should then have ceased to exist or to be a qualifying charitable organization (as hereinafter defined), to one or more qualifying charitable organizations which shall be selected by the Board of Directors of the Corporation. For purposes of these Articles of Incorporation, the term "qualifying charitable organization" shall mean a corporation, fund or foundation which is created in the United States, any state or territory, the District of Columbia, or any possession of the United States, organized and operated exclusively for religious, charitable, scientific, literary or educational purposes which then qualifies as exempt from taxation under the provisions of Section 501(c)(3) of the Code, is then described in Section 170(c)(2) of the Code and is then other than a private foundation pursuant to Section 509(a) of the Code. In the event that for any reason upon the dissolution of the Corporation the Directors of the Corporation shall fail to act in the manner herein provided within a reasonable time, the senior judge of the Superior Court of Durham County, North Carolina, shall make such distributions as herein provided upon the application of one or more persons having an official position with the Corporation or Duke University.

IX.

A. The affairs of the Corporation shall be managed by a Board of Directors consisting of at least thirteen (13) but no more than twenty two (22) voting members. The members of the Board of Directors of the Corporation, other than the *ex officio* members described in IX.B. below, shall be nominated by the Board of Directors of the Corporation, and shall be appointed by the Board of Trustees of Duke University. Members of the Board of Directors of the Corporation shall be subject to removal at the discretion of the Board of Trustees of Duke University in accordance with the Bylaws of the Corporation.

B. The Board of Directors shall include five (5) *ex officio* members, who shall be the individuals serving as President of Duke University, the Chancellor for Health Affairs of Duke University / President and Chief Executive Officer of the Corporation, the Chair of the Board of Trustees of Duke University, the Dean of the Duke University School of Medicine and the Chair of the Board of the Duke University School of Medicine faculty practice plan. A minimum of

eight (8) members of the Board of Directors shall be current or former Duke University Trustees. At least one member of the Board of Directors shall be a Chair of a Clinical Department in the Duke University School of Medicine. The remainder of the members of the Board of Directors shall be individuals selected to serve on the basis of their ability to contribute to the governance of the Corporation.

C. The exact number of the members of the Board of Directors, and the nomination process by which individuals are nominated to the Duke University Board of Trustees for appointment, shall be as provided from time to time by the Bylaws of the Corporation, except that the minimum and maximum number of the members and the composition of the initial Board of Directors as defined by Articles IX and X of these Articles of Incorporation shall remain as set forth herein.

X.

The initial Board of Directors of the Corporation shall serve until the Corporation receives recognition from the Internal Revenue Service that it is exempt from Federal income tax under Sections 501(a) and 501(c)(3) of the Code, and shall consist of three (3) members whose names and addresses are as follows:

David B. Adcock
Duke University / Box 90079
011 Allen Building
Durham, North Carolina 27708-0079

William J. Donelan
Duke University Medical Center
M105A Davison Building
Box 3701 DUMC
Durham, North Carolina 27710-3701

Ralph McCaughan
Duke University / Box 90079
011 Allen Building
Durham, North Carolina 27708-0079

XI.

No Director or Officer of the Corporation shall be personally liable to the Corporation for monetary damages or breach of his or her fiduciary duty or other duty as a Director or Officer; provided that this provision shall eliminate or limit the liability of an individual only to the extent permitted from time to time by the North Carolina Nonprofit Corporation Act or any successor law or laws.

XII.

These Articles of Incorporation may be amended at any time in the manner provided in the North Carolina Nonprofit Corporation Act (or the corresponding provisions of any future North

Carolina nonprofit corporation law) by the affirmative vote of two-thirds (2/3) of the Directors then in office and the approval of the Board of Trustees of Duke University; provided, however, that no amendment may be made which would cause the Corporation no longer to be described as a qualifying charitable organization.

XIII.

A. The address of the principal office of the Corporation is 2400 Pratt Street, Suite 4000, Durham, Durham County, North Carolina 27710.

B. The address of the registered office of the Corporation is 2400 Pratt Street, Suite 4000, Durham, Durham County, North Carolina 27710.

C. The registered agent of the Corporation at the registered office of the Corporation described in XIII.B. above is David B. Adcock.

XIV.

The name and address of the incorporators are:

David B. Adcock
Duke University / Box 90079
011 Allen Building
Durham, North Carolina 27708-0079

William J. Donelan
Duke University Medical Center
M105A Davison Building
Box 3701 DUMC
Durham, North Carolina 27710-3701

Ralph McCaughan
Duke University / Box 90079
011 Allen Building
Durham, North Carolina 27708-0079

Moira Ann Rynn

Consulting Professor in the Department of Psychiatry and Behavioral Sciences

Dr. Rynn is Chair for the Department of Psychiatry and Behavioral Sciences at Duke University School of Medicine. She is an internationally-renowned expert in the treatment of pediatric mood and anxiety disorders. She has spent her career focused on improving treatments for children, adolescents, and young adults with treatment refractory mood and anxiety disorders. Her most recent studies have examined novel augmentation treatment strategies for pediatric Obsessive-Compulsive Disorder and treatment models for adolescent depression in the primary care setting. Dr. Rynn received her medical degree from Rutgers University. She completed her internship and residency in psychiatry at the University of Pennsylvania Perelman School of Medicine and served as Chief Resident. After completing her adult psychiatry training, she completed a Child and Adolescent Psychiatry Fellowship at the Children's Hospital of Philadelphia followed by a Neuropsychopharmacology Research Fellowship sponsored by the NIMH at the University of Pennsylvania Perelman School of Medicine. Prior to joining Columbia University, Dr. Rynn was medical director of the Mood and Anxiety Disorders Section of the Department of Psychiatry at the University of Pennsylvania Perelman School of Medicine. (less)

Current Appointments & Affiliations

- Consulting Professor in the Department of Psychiatry and Behavioral Sciences, Psychiatry, Child & Family Mental Health & Community Psychiatry, Psychiatry & Behavioral Sciences 2017
- Chair of Psychiatry and Behavioral Sciences, Psychiatry & Behavioral Sciences, Clinical Science Departments 2017
- Interim Co-Division Director of Behavioral Medicine and Neurosciences, Psychiatry & Behavioral Sciences, Behavioral Medicine & Neurosciences, Psychiatry & Behavioral Sciences 2020

Contact Information

moira.rynn@duke.edu

Background

Education, Training, & Certifications

Postdoctoral Research Fellow, Psychiatry, National Institutes of Health 1997 - 1998

Resident, Division of Child and Adolescent Psychiatry, Psychiatry, Children's Hospital of Philadelphia 1995 - 1997

Chief Resident, Psychiatry, Psychiatry, University of Pennsylvania, School of Medicine 1994 - 1995

Resident, Adult Psychiatry, Psychiatry, University of Pennsylvania, School of Medicine 1992 - 1995

Intern in Psychiatry, Psychiatry, University of Pennsylvania, School of Medicine 1991 - 1992

M.D., Rutgers, New Jersey Medical School 1991

Previous Appointments & Affiliations

Interim Co-Division Director of General Psychiatry, Psychiatry & Behavioral Sciences, Clinical Science Departments 2019 - 2020

Interim Division Director of Brain Stimulation and Neurophysiology, Psychiatry & Behavioral Sciences, Clinical Science Departments 2019 - 2020

Leadership & Clinical Positions at Duke

Chair, Department of Psychiatry and Behavioral Sciences

Research

External Relationships

Allergen

Boston Children's Hospital

Everett Clinical Reserach

Otsuka Pharmaceuticals

University of California Irvine

Up to Date

This faculty member (or a member of their immediate family) has reported outside activities with the companies, institutions, or organizations listed above. This information has been reported to the health system leadership and, when appropriate, management plans are in place to address potential conflicts of interest.

Publications & Artistic Works

Selected Publications

Academic Articles

Wang, Zhishun, Martine Fontaine, Marilyn Cyr, Moira A. Rynn, Helen Blair Simpson, Rachel Marsh, and David Pagliaccio. "Subcortical shape in pediatric and adult obsessive-compulsive disorder." *Depress Anxiety* 39, no. 6 (June 2022): 504-14. https://doi.org/10.1002/da.23261.

Full Text Link to Item

Bushnell, Greta A., Moira A. Rynn, Stephen Crystal, Tobias Gerhard, and Mark Olfson. "Simultaneous Benzodiazepine and SSRI Initiation in Young People With Anxiety Disorders." *J Clin Psychiatry* 82, no. 6 (October 19, 2021). https://doi.org/10.4088/JCP.20m13863.

Full Text Link to Item

Movaghar, Arezoo, David Page, Krishanu Saha, Moira Rynn, and Jan Greenberg. "Machine learning approach to measurement of criticism: The core dimension of expressed emotion." *J Fam Psychol* 35, no. 7 (October 2021): 1007–15. https://doi.org/10.1037/fam0000906.

Full Text Link to Item

Cyr, Marilyn, David Pagliaccio, Paula Yanes-Lukin, Pablo Goldberg, Martine Fontaine, Moira A. Rynn, and Rachel Marsh. "Altered fronto-amygdalar functional connectivity predicts response to cognitive behavioral therapy in pediatric obsessive-compulsive disorder." *Depress Anxiety* 38, no. 8 (August 2021): 836–45. https://doi.org/10.1002/da.23187.

Full Text Link to Item

Weidle, Bernhard, Tord Ivarsson, Fernando R. Asbahr, Rosa Calvo, David Mataix-Cols, Moira A. Rynn, and Eric A. Storch. "Specialty knowledge and competency standards for pharmacotherapy for pediatric obsessive-compulsive disorder." *Psychiatry Res* 299 (May 2021): 113858. https://doi.org/10.1016/j.psychres.2021.113858.

Full Text Link to Item

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Book Sections

Strawn, J. R., E. T. Dobson, A. B. Ramesh, S. A. Berger, and M. A. Rynn. "Pharmacologic treatment of pediatric anxiety disorders." In *Pediatric Anxiety Disorders*, 359–84, 2019. https://doi.org/10.1016/B978-0-12-813004-9.00017-7.

Full Text

Heleniak, C. M., T. Kaur, K. D. Ghalib, and M. A. Rynn. "Tricyclic Antidepressants and Monoamine Oxidase Inhibitors for the Treatment of Child and Adolescent Psychiatric Disorders." In *Pharmacotherapy of Child and Adolescent Psychiatric Disorders: Third Edition*, 105–29, 2012. https://doi.org/10.1002/9781119958338.ch7.

Full Text

Vidair, H. B., and M. A. Rynn. "Childhood anxiety disorders: Best treatment options and practice." In *Anxiety Disorders: Theory, Research, and Clinical Perspectives*, 306–22, 2010. https://doi.org/10.1017/CBO9780511777578.029.

Full Text

Conference Papers

Duarte, Cristiane S., Chiaying Wei, Shuai Wang, Anne M. Albano, Moira A. Rynn, John T. Walkup, and Mark Olfson. "3.21 DSM-5 ANXIETY DISORDERS AMONG YOUNG ADULTS IN THE UNITED STATES." In *Journal of the American Academy of Child &Amp; Adolescent Psychiatry*, 55:S148–49. Elsevier BV, 2016. https://doi.org/10.1016/j.jaac.2016.09.153.

Full Text

Duarte, Cristiane S., Maria C. Zerrate, and Moira A. Rynn. "47.0 Bringing Evidence-Based Treatment to Emerging Adults With Anxiety Disorders in Three Clinical Settings: The Youth Anxiety Center." In *Journal of the American Academy of Child &Amp; Adolescent Psychiatry*, 55:S71-72. Elsevier BV, 2016. https://doi.org/10.1016/j.jaac.2016.07.719.

Full Text

Fitzgerald, Kate D., Rachel Marsh, and Moira A. Rynn. "21.0 Abnormal Neural Substrate for Performance Monitoring in Pediatric Obsessive-Compulsive Disorder: Implications for Understanding Treatment Response." In *Journal of the American Academy of Child &Amp; Adolescent Psychiatry*, 55:S290-S290. Elsevier BV, 2016. https://doi.org/10.1016/j.jaac.2016.07.237.

Full Text

Marsh, Rachel, Emily J. Steinberg, Pablo H. Goldberg, Paula Yanes-Lukin, Dylan Braun, Chiaying Wei, Christa D. Labouliere, and Moira A. Rynn. "21.1 COGNITIVE-BEHAVIORAL THERAPY-BASED CHANGES IN CONTROL AND REWARD CIRCUITS IN PEDIATRIC OBSESSIVE-COMPULSIVE DISORDER." In *Journal of the American Academy of Child &Amp; Adolescent Psychiatry*, 55:S290-S290. Elsevier BV, 2016. https://doi.org/10.1016/j.jaac.2016.07.238.

Full Text

Mufson, Laura, and Moira A. Rynn. "Interpersonal Psychotherapy for Depression: Understanding the Core of the Interpersonal Psychotherapy for Depressed Adolescents Model and Its Adaptations." In *Journal of the American Academy of Child &Amp; Adolescent Psychiatry*, 55:S38-S38. Elsevier BV, 2016. https://doi.org/10.1016/j.jaac.2016.07.582.

Full Text

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Scholarly, Clinical, & Service Activities

Service to the Profession

Participant. Faculty Short Course on Improving Departmental Climate. Duke Office of Faculty Advancement & Duke Office of Institutional Equity. August 2, 2021 - August 5, 2021 2021

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Wei Jiang

Professor of Psychiatry and Behavioral Sciences

Professor of Medicine

Affiliate, Duke Global Health Institute

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Dr. Wei Jiang leads the Neuropsychocardiology laboratory at Duke University Medical Center. Dr. Jiang's main research interests include understanding the interplay between the mind-brain activity and cardiovascular system, and discovering interventions that modify the negative impact of negative emotions on the cardiovascular system. Her research covers the spectrum of epidemiological cohort study, translational investigation, clinical trials, and implementational evaluation. Another research area of Dr. Jiang is to investigate effective methods for mental health task shifting in low and middle income countries, particularly aiming in China.

Education

- M.D. 1982 - Binzhou Medical School (China)

Grants

- Exercise and Pharmacotherapy for Anxiety in Cardiac Patients awarded by National Institutes of Health 2015 - 2022
- Biomarkers of Mental Stress Induced Myocardial Ischemia and CHD Prognosis awarded by National Institutes of Health 2014 - 2019
- Mental Stress-Induced Left Ventricular Dysfunction and Mitochondrial Dysfunction in Women awarded by National Institutes of Health 2018 - 2018
- 2/3 Multi-Site - Omega-3 for Co-Morbid Depression & HF Treatment (OCEAN) awarded by Thomas Jefferson University 2015 - 2017
- 3/3 Multi-Site Omega-3 for Co-Morbid Depression & HF Treatment (OCEAN) awarded by University of North Carolina - Chapel Hill 2015 - 2017
- 1/3 Multi-Site - Omega-3 for Co-Morbid Depression & HF Treatment (OCEAN) awarded by National Institutes of Health 2013 - 2017
- Nocturnal Deterusor Overactivity In Overactive Bladder Syndrome awarded by National Institutes of Health 2010 - 2014
- Responses of Myocardial Ischemia to Sertraline Treatment awarded by National Institutes of Health 2006 - 2013
- Exercise, Depression, and Cardiac Risk awarded by National Institutes of Health 2006 - 2012
- Safety and Efficacy of Sertraline for Depression CHF awarded by National Institutes of Health 2003 - 2011

Grants

- Safety and Efficacy of Sertraline for Depression CHF awarded by National Institutes of Health 2003 - 2011
- Development of the Inventory of Depressive Symptomatology awarded by National Institutes of Health 2003 - 2006
- Stress & Myocardial Ischemia: Mechanisms & Treatment awarded by National Institutes of Health 1998 - 2006
- Inflammatory Biomarkers in Depressed CHF Patients awarded by National Institutes of Health 2003 - 2004

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Alenezi, Fawaz, Beverly H. Brummett, Stephen H. Boyle, Zainab Samad, Michael A. Babyak, Nabil Alzaeim, Jennifer Wilson, et al. "Usefulness of Myocardial Annular Velocity Change During Mental Stress to Predict Cardiovascular Outcome in Patients With Coronary Artery Disease (From the Responses of Mental Stress-Induced Myocardial Ischemia to Escitalopram Treatment Trial)." *Am J Cardiol* 120, no. 9 (November 1, 2017): 1495–1500. https://doi.org/10.1016/j.amjcard.2017.07.039.

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Past Appointments

- Assistant Professor of Medicine
- Associate Professor of Psychiatry and Behavioral Sciences

Publications

Sun, Julia L., Stephen H. Boyle, Zainab Samad, Michael A. Babyak, Jennifer L. Wilson, Cynthia Kuhn, Richard C. Becker, et al. "Mental stress-induced left ventricular dysfunction and adverse outcome in ischemic heart disease patients." *Eur J Prev Cardiol* 24, no. 6 (April 2017): 591–99. https://doi.org/10.1177/2047487316686435.

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Past Appointments

- Assistant Professor of Medicine
- Associate Professor of Psychiatry and Behavioral Sciences
- Professor of Psychiatry and Behavioral Sciences
- Assistant Professor of Medicine
- Assistant Professor of Psychiatry and Behavioral Sciences
- Associate Professor of Psychiatry and Behavioral Sciences

Publications

Harrison, Robert W., Richard Becker, Thomas Ortel, Maggie Kuchibhatla, Stephen Boyle, Zainab Samad, Eric Velazquez, Jennifer Wilson, Cynthia Kuhn, and Redford Williams. "ASSOCIATION BETWEEN PLATELET AGGREGATION AND MENTAL STRESS INDUCED MYOCARDIAL ISCHEMIA: RESULTS FROM THE REMIT TRIAL." In *Journal of the American College of Cardiology*, 61:E1135–E1135. Elsevier BV, 2013. https://doi.org/10.1016/s0735-1097(13)61135-3.

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Publications

Jiang, Wei, Harry Oken, Mona Fiuzat, Linda K. Shaw, Carolyn Martsberger, Maragatha Kuchibhatla, Rima Kaddurah-Daouk, et al. "Plasma omega-3 polyunsaturated fatty acids and survival in patients with chronic heart failure and major depressive disorder." *J Cardiovasc Transl Res* 5, no. 1 (February 2012): 92–99. https://doi.org/10.1007/s12265-011-9325-8.

Jiang, Wei, Eric J. Velazquez, Zainab Samad, Maragatha Kuchibhatla, Carolyn Martsberger, Joseph Rogers, Redford Williams, et al. "Responses of mental stress-induced myocardial ischemia to escitalopram treatment: background, design, and method for the Responses of Mental Stress Induced Myocardial Ischemia to Escitalopram Treatment trial." *Am Heart J* 163, no. 1 (January 2012): 20–26. https://doi.org/10.1016/j.ahj.2011.09.018.

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Past Appointments

- Assistant Professor of Medicine
- Associate Professor of Psychiatry and Behavioral Sciences

bypass grafting.” *Clin Cardiol* 33, no. 6 (June 2010): E94–98. https://doi.org/10.1002/clc.20621.

Steffens, David C., David C. Wei Jiang, K Ranga R. Krishnan, Edward D. Karoly, Matthew W. Mitchell, Christopher M. O’Connor, and Rima Kaddurah-Daouk. “Metabolomic differences in heart failure patients with and without major depression.” *J Geriatr Psychiatry Neurol* 23, no. 2 (June 2010): 138–46. https://doi.org/10.1177/0891988709358592.

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Past Appointments

- Assistant Professor of Medicine
- Associate Professor of Psychiatry and Behavioral Sciences
- Professor of Psychiatry and Behavioral Sciences
- Assistant Professor of Medicine
- Assistant Professor of Psychiatry and Behavioral Sciences
- Associate Professor of Psychiatry and Behavioral Sciences
- Associate Professor of Medicine

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- Stress May Be Harder on Women's Hearts than Men's
- Stress May Be Harder on Women's Hearts than Men's

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Duke Psychiatry & Behavioral Sciences
Duke University School of Medicine

CONFIDENTIAL

December 18, 2020

To: Dr. Howard Bauchner

Re: *JAMA*. 2013;309(20):2139-2149. doi:10.1001/jama.2013.5566

Dear Dr. Bauchner,

As director of the Psychiatry Clinical Research Unit (CRU), I am contacting you regarding the manuscript published in *JAMA* on May 22, 2013 entitled, "Effect of escitalopram on mental stress-induced myocardial ischemia: Results of the REMIT trial." The REMIT trial examined the effects of 6 weeks of escitalopram treatment *vs.* placebo on mental-stress-induced myocardial ischemia (MSIMI).

A recent institutional internal review determined that 26 (or 20.5%) of the 127 study participants enrolled in the trial did not meet all inclusion/exclusion criteria specified in the protocol. For example, one key inclusion criteria required that participants be physically capable of performing an exercise stress test and, if applicable, withhold beta-blocker medication prior to the test. However, it was discovered that a group of participants did not meet this inclusion criteria. That is, they were physically unable to perform the required exercise stress tests and/or did not withhold their beta-blocker medication prior to the exercise stress test.

An independent re-analysis of the study results using data from only those participants who met all inclusion/exclusion criteria showed that some of the results reported in the publication were no longer statistically significant. In particular, the difference in the incidence of MSIMI among participants receiving escitalopram compared to those receiving placebo did not reach statistical significance, and the overall magnitude of the effect was smaller. For your review, a comparison of the results of the re-analysis to those published in Table 4 of the JAMA manuscript are provided in Appendix A (see below) of this document.

Additionally, the following errors were identified:

a. The number of participants listed in Table 1 as "total with history of diabetes" was actually "total **without** history of diabetes."
b. What was presented in the manuscript as resting heart rate was actually weight in kg.
c. What was presented as weight in kg was actually weight in lbs.
d. The standard deviations for "trait anxiety" in Table 2 were incorrect.
e. What was labeled in Table 2 as resting negative affect and resting positive affect was actually mean negative affect and mean positive affect.

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f. The *p*-values in Table 3 were labeled as Fischer's exact tests, but were actually chi-square tests.
g. The data presented in Table 4 included an extra placebo patient.
h. The models in Table 5 were not adjusted for age even though the footnote indicates that they were.

Based on the information above, we believe the publication may need to be corrected or retracted. We are seeking your guidance and recommendations on next steps.

If you have questions or need additional information, please feel free to contact me at your earliest convenience. I can be reached by phone at (919) 200-9885 and by email at compt004@duke.edu.

Sincerely,

Scott Compton, PhD
Associate Professor
Director, Clinical Research Unit (CRU)
Department of Psychiatry and Behavioral Sciences, Duke University School of Medicine
Associate Professor of Psychology & Neuroscience, Duke University

CC: Moira Rynn MD, Chair, Department of Psychiatry and Behavioral Sciences, Duke University School of Medicine
Geeta Swamy MD, Associate Vice President for Research, Duke University; Vice Dean for Scientific Integrity, Duke University School of Medicine
Donna Kessler PhD, Research Integrity Officer, Duke University

APPENDIX A

Table 4. MSIMI Defined by Wall Motion Abnormality and/or LVEF at Baseline and Endpoint

	From Original Publication (N=127)				From Reanalysis After Removing Patients Failing to Meet Inclusion/Exclusion Criteria (N=101)			
Variable	**Escitalopram**	**Placebo**	**OR (95% CI)**	**P-value**	**Escitalopram**	**Placebo**	**OR (95% CI)**	**P-value**
Baseline, n (%)								
Overall MSIMI	63/64 (98.4%)	63/63 (100%)		>.99	51/52 (98.1%)	49/49 (100%)		>.99[1]
Wall motion abnormality only	37/64 (57.8%)	42/63 (66.7%)			27/52 (51.9%)	35/49 (71.4%)		
LVEF reduction ≥ -8% only	9/64 (14.1%)	9/63 (14.3%)			8/52 (15.4%)	8/49 (16.3%)		
Both	17/64 (26.6%)	12/63 (19.1%)			16/52 (30.8%)	6/49 (12.2%)		
Endpoint, n (%)								
Overall MSIMI	37/56 (66.1%)	47/56 (83.9%)	2.68 [1.09, 6.61]	.03	29/46 (63.0%)	34/44 (77.3%)	1.99 [0.79, 5.02]	.14
Adjusted per-protocol, n (%)			2.57 [0.99, 6.66]	.05			2.16 [0.80, 5.83]	.13
Wall motion abnormality (WMA) only	22/56 (39.3%) [30.2, 48.3]	32/56 (57.1%) [47.9, 66.3]			16/46 (34.8%) [21.0, 48.6]	23/44 (52.3%) [37.51, 67.0]		
LVEF reduction ≥ -8% only	3/56 (5.4%) [1.2, 9.5]	4/56 (7.1%) [2.3, 11.9]			2/46 (4.3%) [0.5, 14.8]	2/44 (4.6%) [0.56, 15.5]		
Both	12/56 (21.4%) [13/8, 29.0]	11/56 (19.6%) [12.3, 27.0]			11/46 (23.9%) [11.6, 36.2]	9/44 (20.4%) [8.54, 32.4]		
Imputed primary end point, %								
No MSIMI	34.2% [31.6, 36.8]	17.5% [15.4, 19.6]	2.62 [1.06, 6.44]	.04	38.9% [24.3, 53.4]	24.5% [10.3, 38.7]	1.97 [0.77, 5.02]	.16

1. P-value from Fisher's exact test.

Note: With the reduced sample, the lower rate of MSIMI at endpoint in escitalopram participants does not reach statistical significance and the magnitude of the effect is attenuated. The odds ratio for the association between escitalopram treatment and no MSIMI was published to be 2.68 in completers (2.62 when imputed) and we observe an odds ratio of 1.99 in the reduced sample (1.97 when imputed). If a reason is not found and the endpoint is changed for the one placebo patient who the manuscript classified as having endpoint MSIMI but whom we do not see the evidence for that classification, then the odds ratio in the original manuscript would have been 2.36 in completers. P-values that were less than 0.05 in the publication are greater than 0.1 in the subset deemed eligible.

Duke University Health System

Wei Jiang, M.D. Professor
Department of Psychiatry & Behavioral Sciences
Department of Medicine

December 18, 2020

Howard Bauchner, MD
Editor in Chief
JAMA
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bauchner@bu.edu

Re: *JAMA*. 2013;309(20):2139-2149. doi:10.1001/jama.2013.5566

Dear Dr. Bauchner,

On behalf of myself and my colleagues, I am contacting you regarding the May 22, 2013 *JAMA* publication entitled, "Effect of escitalopram on mental stress-induced myocardial ischemia: Results of the REMIT trial." The REMIT (Responses of Mental Stress Induced Myocardial Ischemia to Escitalopram Treatment) trial primarily examined the effects of 6 weeks of Escitalopram vs. placebo on mental-stress-induced myocardial ischemia (MSIMI).

I have been requested to bring to your attention the following corrections to the 2013 publication. Errors with the corrections are as follows:

a. The subtitle of "with history of diabetes mellitus" in Table 1 should have been "no history of diabetes mellitus" and the number of participants under the "Total" column for this variable should be 35/127 (27.6%);

b. The unit for Weight in Table 2 was pounds, not Kg; and

c. The standard deviations for "trait anxiety" in Table 2 for escitalopram should be (10.8) instead of (0.9), and for placebo should be (10.6) instead of (0.9).

These errors were unintentional and do not implicate any of the findings of the REMIT Trial conducted between 2006 and 2011 at Duke University (DU). The REMIT Investigative team stands by the original findings of the study as published with the above corrections.

I also provide the following for your information only because issues were raised during the re-evaluations of the study data which occurred internally at DU between April 2018 and October 2019. These re-evaluations of the REMIT study were originally and apparently initiated by the chair of the Psychiatry Department of the DU School of Medicine Dr. Moira Rynn approximately 12 years after the beginning of the study (2006) and approximately 7 years after the conclusion of the study (2011).

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The original protocol was published at Am Heart J 2012; 163:20-6 and provided 2 inclusion and 11 exclusion criteria. All participants in the study were qualified with regard to the 2 inclusion and 11 exclusion criteria when they initially provided study consent. In addition, the protocol also originally required exercise testing in addition to mental stress testing. As you are no doubt aware, "randomized controlled trials (RCT) often suffer from two major complications, i.e., noncompliance and missing outcomes." S. Gupta, Perspect Clin Res. 2011 Jul-Sep; 2(3): 109–112. Analysis of the data in an RCT thus utilizes the ITT analysis (intention to treat) of the entire patient population randomized as well as analysis of the reduced subset of the patients who completed the study. The 2013 JAMA article presented the ITT cohort data, and as stated above, and the investigative team stands by that data and its analysis.

Because of the waiting period between the time consent was given and when the subjects presented for baseline stress testing, some of the patients who had provided consent were determined to be unable or unwilling to undergo exercise stress testing or withhold anginal medications or beta-blockers due to safety concerns related to high blood pressure and/or tachycardia. Those patients who could or did not engage in beta-blocker withdrawal or exercise testing were discussed among the key investigators and REMIT data safety monitoring board (DSMB) either prospectively, or immediately after, the mental stress testing. It was determined that protocol deviations needed to be approved to allow for the participation of those patients in the study. [1] The REMIT team received waivers for all 26 participants from the REMIT DSMB chairman. The DSMB was charged with notifying the IRB of the waivers under the research regulatory rules of clinical trials conducted between 2006 and 2011. These research regulatory rules allowed for the change in the protocol to protect patient safety given that the change did not jeopardize the primary goal of the study.

To recapitulate:

- The deviation from the original protocol was permitted in order to ensure patient safety.
- These changes in the original protocol did not in any way adversely affect the primary goal of the REMIT study.
- All the amendments were reviewed with and supported by the REMIT DSMB Chair.
- No safety concerns were raised by the independent DSMB throughout the trial.
- Subsequent review of the REMIT study data from the 2006-2011 conducted between April 2018 and October 2019 found no patient safety concerns or any research misconduct.
- The Duke IRB also concluded that there was no Unanticipated Problem Involving Risk to Subjects or Others (UPIRTSO).

[1] Twenty-one of the 26 REMIT participants had the beta-blocker withholding issues and 8 of the 26 participants were not able to engage with exercise testing during the baseline stress testing.

- The 2013 JAMA article presented the ITT cohort data and the investigative team stands by that data and its analysis.

I would be happy to speak to you or your team further regarding this matter.

Sincerely,

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CC: REMIT co-investigators and REMIT DSMB Chair

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Duke Psychiatry & Behavioral Sciences
Duke University School of Medicine

CONFIDENTIAL

December 22, 2020

To: Eric Velazquez, Maragatha Kuchibhatla, Zainab Samad, Stephen Boyle, Cynthia Kuhn, Richard Becker, Thomas Ortel, Redford Williams, Joseph Rogers, Christopher O'Connor

Re: *JAMA*. 2013;309(20):2139-2149. doi:10.1001/jama.2013.5566

Dear Co-Authors,

As director of the Psychiatry Clinical Research Unit (CRU), I am contacting you regarding the manuscript published in *JAMA* on May 22, 2013 entitled, "Effect of escitalopram on mental stress-induced myocardial ischemia: Results of the REMIT trial."

A recent institutional internal review determined that 26 (or 20.5%) of the 127 study participants enrolled in the trial did not meet all inclusion/exclusion criteria specified in the protocol. For example, one key inclusion criteria required that participants be physically capable of performing an exercise stress test and, if applicable, withhold beta-blocker medication prior to the test. However, it was discovered that a group of participants did not meet this inclusion criteria. That is, they were physically unable to perform the required exercise stress tests and/or did not withhold their beta-blocker medication prior to the exercise stress test.

An independent re-analysis of the study results using data from only those participants who met all inclusion/exclusion criteria showed that some of the results reported in the publication were no longer statistically significant. In particular, the difference in the incidence of MSIMI among participants receiving escitalopram compared to those receiving placebo did not reach statistical significance, and the overall magnitude of the effect was smaller. For your review, a comparison of the results of the re-analysis to those published in Table 4 of the JAMA manuscript are provided in Appendix A (see below) of this document.

Additionally, the following errors were identified:

a. The number of participants listed in Table 1 as "total with history of diabetes" was actually "total **without** history of diabetes."
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f. The *p*-values in Table 3 were labeled as Fischer's exact tests, but were actually chi-square tests.
g. The data presented in Table 4 included an extra placebo patient.
h. The models in Table 5 were not adjusted for age even though the footnote indicates that they were.

Based on the information above, the department has been instructed to submit a notification to the Editor JAMA seeking guidance and recommendations on next steps. As a co-author you are also being being notified.

If you have questions or need additional information, please contact me at your earliest convenience. I can be reached by phone at (919) 200-9885 and by email at compt004@duke.edu.

Sincerely,

Scott Compton, PhD
Associate Professor
Director, Clinical Research Unit (CRU)
Department of Psychiatry and Behavioral Sciences, Duke University School of Medicine
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CC: Wei Jiang, MD
Moira Rynn MD, Chair, Department of Psychiatry and Behavioral Sciences, Duke University School of Medicine
Geeta Swamy MD, Associate Vice President for Research, Duke University; Vice Dean for Scientific Integrity, Duke University School of Medicine
Donna Kessler PhD, Research Integrity Officer, Duke University

APPENDIX A

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	From Original Publication (N=127)				From Reanalysis After Removing Patients Failing to Meet Inclusion/Exclusion Criteria (N=101)			
Variable	**Escitalopram**	**Placebo**	**OR (95% CI)**	**P-value**	**Escitalopram**	**Placebo**	**OR (95% CI)**	**P-value**
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Wall motion abnormality only	37/64 (57.8%)	42/63 (66.7%)			27/52 (51.9%)	35/49 (71.4%)		
LVEF reduction ≥ -8% only	9/64 (14.1%)	9/63 (14.3%)			8/52 (15.4%)	8/49 (16.3%)		
Both	17/64 (26.6%)	12/63 (19.1%)			16/52 (30.8%)	6/49 (12.2%)		
Endpoint, n (%)								
Overall MSIMI	37/56 (66.1%)	47/56 (83.9%)	2.68 [1.09, 6.61]	.03	29/46 (63.0%)	34/44 (77.3%)	1.99 [0.79, 5.02]	.14
Adjusted per-protocol, n (%)			2.57 [0.99, 6.66]	.05			2.16 [0.80, 5.83]	.13
Wall motion abnormality (WMA) only	22/56 (39.3%) [30.2, 48.3]	32/56 (57.1%) [47.9, 66.3]			16/46 (34.8%) [21.0, 48.6]	23/44 (52.3%) [37.51, 67.0]		
LVEF reduction ≥ -8% only	3/56 (5.4%) [1.2, 9.5]	4/56 (7.1%) [2.3, 11.9]			2/46 (4.3%) [0.5, 14.8]	2/44 (4.6%) [0.56, 15.5]		
Both	12/56 (21.4%) [13/8, 29.0]	11/56 (19.6%) [12.3, 27.0]			11/46 (23.9%) [11.6, 36.2]	9/44 (20.4%) [8.54, 32.4]		
Imputed primary end point, %								
No MSIMI	34.2% [31.6, 36.8]	17.5% [15.4, 19.6]	2.62 [1.06, 6.44]	.04	38.9% [24.3, 53.4]	24.5% [10.3, 38.7]	1.97 [0.77, 5.02]	.16

1. P-value from Fisher's exact test.

Note: With the reduced sample, the lower rate of MSIMI at endpoint in escitalopram participants does not reach statistical significance and the magnitude of the effect is attenuated. The odds ratio for the association between escitalopram treatment and no MSIMI was published to be 2.68 in completers (2.62 when imputed) and we observe an odds ratio of 1.99 in the reduced sample (1.97 when imputed). If a reason is not found and the endpoint is changed for the one placebo patient who the manuscript classified as having endpoint MSIMI but whom we do not see the evidence for that classification, then the odds ratio in the original manuscript would have been 2.36 in completers. P-values that were less than 0.05 in the publication are greater than 0.1 in the subset deemed eligible.

January 21, 2021

JAMA Network
Attn: Dr. Howard Bauchner and Dr. Phil Fontanarosa
330 N Wabash Ave
Chicago, IL 60611

Re: *JAMA*.2013; 309 (20):2139-2149. doi:10.1001/jama.2013.5566

Dear Howard and Phil,

Thank you for allowing me to represent the investigators and present our position regarding the issues concerning the REMIT trial we discussed earlier this week. The investigators only recently, in December of 2020, became aware of the findings of what Scott Compton, Clinical Research Unit Director, Duke Psychiatry and Behavioral Sciences, describes in his letter to you as an "institutional internal review", in December 2020. Dr. Compton's letter to you which purports to summarize the internal review findings are troubling in many regards and are discussed below:

1. The specific details of the "institutional internal review" have not been shared with the investigators, except Dr. Jiang, the principal investigator. Based on what we have learned about how the internal reviews were conducted, we have reason to question the methodology used in them and some of their conclusions.

2. The initial audit undertaken by the Duke Department of Psychiatry Clinical Research Unit (CRU) in April 2018 reviewed documentation on only 10 of the 310 study subjects.

3. Based on the CRU review, Dr. Rynn. The Chair of Psychiatry then requested an additional review by the Duke University Audit, Risk and Compliance Office (OARC).

4. The September 2018 OARC review of some but not all of the REMIT study materials, concluded there were "no significant patient safety concerns." In addition, this review also raised the issue of protocol deviations resulting from the inclusion/exclusion of subjects with regard to the exercise testing and beta blocker usage.

5. The subsequent IRB review on December 26, 2018, also concluded there were no patient safety issues and no "Unanticipated Problems involving Risk to Subjects or Others" (UPIRTSO).

6. In March 2019, two additional reviewers of the data stated that after re-evaluating the datasets and programs used in the JAMA article, "our numbers

are very close to what were published." Even after excluding the 26 subjects who did not undergo exercise testing or discontinuance of beta blockers, the reviewers stated "the results obtained from this reduced patient sample are in general very similar to the results published in JAMA."

7. Finally, a review was conducted by the Duke Standing Committee on Misconduct in Research (SCMR) beginning in March 2019. This review included a re-reading of the original echocardiogram images by an "independent" cardiologist who had not been specifically trained in how to analyze REMIT echo images, had knowledge of the randomization codes, and also who worked alone. The SCMR report issued in October 2019 concluded, again, that there was no evidence of any falsification or fabrication of study records and reiterated concerns regarding protocol deviation.

The internal reviews raise two groups of issues essentially resulting from what are referred to by Scott Compton in his letter "protocol deviations" related to the inclusion/exclusion criteria of exercise testing and beta blocker usage/discontinuance.

These changes only enhanced **patient safety** and had no impact on **data quality** and therefore can be considered Grade One[1] protocol deviations. These two issues are discussed in more detail below and should inform your analysis of Scott Compton's letter.

Patient Safety: Both the OARC report and the subsequent IRB review on December 26, 2018, concluded there were no patient safety issues and no "Unanticipated Problems involving Risk to Subjects or Others" (UPIRTSO).

In addition, the regulatory environment that the investigators conducted the trial between 2006 and 2011 was guided by the federal law policy of the 1572 Statement of Investigator of this investigator initiated, FDA exempt, NIH funded clinical investigation (see attached form FDA-1572). The Duke IRB follows federal law policy under OHRP. Of note, after completion of the REMIT trial, in 2012, the NIH adopted and harmonized the regulatory

[1] Perspect Clin Res. 2016 Jul-Sep; 7(3): 132–136. Assessment and classification of protocol deviations Ravindra Bhaskar Ghooi, Neelambari Bhosale, Reena Wadhwani, Pathik Divate, and Uma Divate ("Deviations from the approved protocol are common and have been noted both in routine management and in research, at differing frequency. . . . It is accepted that deviations vary in their incidence and impact and have also been classified accordingly." Classifications range from "Grade 1: No impact on data quality or patient safety; Grade 2: Minor impact on data quality; Grade 3: Minor impact on patient safety; Grade 4: Major impact on data quality or patient safety; Grade 5: Leading to patient/(s) death."

requirements of the FDA for NIH investigator initiated trials. In the REMIT trial, all patients signed the informed consent document. Between informed consent and randomization, patients underwent a number of procedures unless safety concerns were brought forth to the Chief Medical Officer (cardiologist) of the trial and reviewed by the Data Safety Monitoring Board (DSMB) chairman. Protocol deviations in up to 26 patients (there is not agreement on this number) were related to safety and protection of the study patients from harm and did not require prospective waivers from the IRB as per the enclosed 1572 regulatory document that the investigative group abided by and looked to for guidance. ("I agree to conduct the study(ies) in accordance with the relevant, current protocol(s) and will only make changes in a protocol after notifying the sponsor, except when necessary to protect the safety, rights, or welfare of subjects").

It is also difficult, in my opinion and that of all of the investigators, for the non-physician auditors to determine the intentions of the study team 10-15 years later as the CMO and DSMB records as well as other parts of the trial database were not retained or reviewed by the auditors given that the that records retention requirement is only 6 years and the reviews began well after that period.

For example, maintenance of beta blocker therapy may have occurred and appeared to auditors to be an exclusion criteria deviation. In actuality it was not a deviation, because the patients were maintained on these medicines for safety reasons to maintain blood pressure and/or heart rate control. This level of critical thinking cannot be reconstructed with incomplete records 10-15 years later. (The study began in 2006 and conclusions are being drawn now in 2021). The investigators believe that they did not violate regulatory policy and acted solely to promote safety. Neither the time nor do we believe the 26 patient cohorts are the correct numbers who had protocol deviations on the two exclusion criteria.

Data Quality: Scott Compton's letter to you and the internal reviews themselves of the protocol deviations related to the two exclusion criteria 10-15 years after the study was conducted fail to take into account **the confirmation of the published findings in the intention to treat cohort.**

There is no scientific basis to consider the 127-26 (101) patient subset instead of the 127 intention to treat cohort as the primary endpoint analysis set. The auditors confirmed the intention to treat results that are presented in the publication. The investigators strongly believe that one cannot remove 26 patients based on the above methodology when the randomization codes were known to the auditors and the blind of the review was not maintained. This process violates good scientific and statistical practice methodology of randomized controlled clinical trials. The intention to treat cohort was

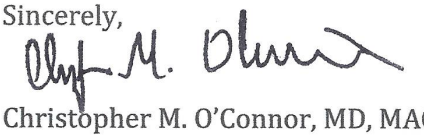
chosen as representing the most conservative approach and the least likely to be contaminated by unintended bias.

As an unplanned exploratory analysis, the odds ratios and confidence intervals in this 101 patient subgroup are consistent with the published results and only suffer from a type 2 error of reduced power from a reduced sample size.

Finally, the investigators agree that 8 variables of over 1000 data elements (0.8%) audited were unintentional errors of transcription or data element transfer. While this is consistent with the error rate of this type of trial, we are not happy that this occurred. Notwithstanding that the the Department of Psychiatry statistician and co-author was charged with final review and proofing of all data elements prior to publication, we as a group of investigators and authors take responsibility for these errors and believe that corrections should be made. I would also not that techniques for trial standards to improve data transcription errors (double data entry and statistical data monitoring) have improved significantly for NIH funded trials since 2006 when the study began.

In conclusion, Scott Compton's suggestion that the article be retracted has no basis in fact or science and the investigators strongly resist this suggestion. As stated above, however, we do believe that a notice of correction is appropriate as the publication contained data errors, as I believe were contained in Dr. Jiang's letter to you on our behalf. Again, I want to thank you for taking these serious issues under consideration and allowing the investigative group to provide additional clarification.

Sincerely,



Christopher M. O'Connor, MD, MACC, FESC, FHFSA, FHFA
Senior Investigator, REMIT Trial
Professor of Medicine, Duke University

Duke | Office of Scientific Integrity

March 18, 2022

VIA E-MAIL ONLY
Phil B. Fontanarosa, MD, MBA
Interim Editor in Chief
JAMA and the JAMA Network

Re: REMIT Trial

Dr. Fontanarosa,

The article by Jiang and colleagues titled "Responses of Myocardial Ischemia to Escitalopram Treatment (REMIT)"[1] published in the March 22, 2013 issue of JAMA included the results from an original investigation conducted at Duke University from 2007 to 2011. The main goal of this double-blind, placebo-controlled, randomized clinical trial was to evaluate the effects of 6 weeks of escitalopram treatment on mental stress-induced myocardial ischemia (MSIMI) in adults with clinically stable coronary heart disease (CHD).

A departmental review of this study conducted in 2018 and a subsequent institutional audit also conducted in 2018 concluded that the trial was not conducted in accordance with the protocol approved by the Duke Health Institutional Review Board (IRB). Although no evidence was found that the investigative team altered study records or information presented in the article, it was identified that individuals were included in the analysis that did not meet enrollment criteria as provided in the IRB approved protocol.

Re-analysis of the primary outcome data (by an independent statistical team) including only participants who met all IRB-approved inclusion/exclusion criteria (n=101; 52 in the escitalopram group; 49 in the placebo group) showed that some of the differences reported in the original article [1] (based on 127 participants: 64 in the escitalopram group; 63 in the placebo group) were no longer statistically significant. In particular, the difference in incidence of no

[1] Jiang W, Velazquez EJ, Kuchibhatla M, et al. Effect of escitalopram on mental stress–induced myocardial ischemia: results of the REMIT trial. *JAMA.* 2013;309(20):2139–2149. doi:10.1001/jama.2013.5566

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MSIMI among participants who were receiving escitalopram vs those receiving placebo was no longer statistically significant, changing from 34.2% with escitalopram vs 17.5% with placebo; OR 2.62 (95% CI 1.06 - 6.44; *P*=.04) in the original publication (Table 4 in the article, imputed primary end point) to 38.9% vs 24.5%; OR 1.97 (95% CI 0.77 - 5.02; *P*=.16) in the re-analysis.

We recommend correction of the published study results using only data and information from participants who met the IRB-approved inclusion/exclusion criteria in the protocol.

Sincerely,

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Annette Flanagin, RN, MA, FAAN, Executive Managing Editor
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April 8, 2021

Dear Drs. Bauchner and Flanagin:

This email is to update you on the response requested by Dr. Bauchner in his email of March 24, 2021.

I am still in the process of gathering the requested IRB documentation. I have been able to obtain much of it, but am still missing the IRB approvals from intermittent years of the study.

In addition, I am continuing to coordinate a response from my co-authors as requested regarding the evaluation of the REMIT study data by the CRU of psychiatry department which excluded data from participants which the JAMA article included. As stated previously, the data analysis in the JAMA article by the co-authors used the intention-to-treat analysis (McCoy 2017*) because it allows the "investigator (or consumer of the medical literature) to draw accurate (unbiased) conclusions regarding the effectiveness of an intervention. This method preserves the benefits of randomization, which cannot be assumed when using other methods of analysis."

I hope to have a final response to you by Friday, April 16. Thank you for your patience.

Sincerely,

Jan Wei Jiang

* C. Eric McCoy, MD, MPH. Understanding the Intention-to-treat Principle in Randomized Controlled Trials. West J Emerg Med. 2017 Oct; 18(6): 1075–1078. Published online 2017

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Department of Psychiatry & Behavioral Sciences
Department of Medicine

Sep 18. doi: 10.5811/westjem.2017.8.35985 PMCID: PMC5654877 PMID: 29085540 (See specified quote from the article below in Italic)

" . . . [P]atients in clinical trials do not always adhere to the protocol. Excluding patients from the analysis who violated the research protocol (did not get their intended treatment) can have significant implications that impact the results and analysis of a study. Intention-to-treat analysis is a method for analyzing results in a prospective randomized study where all participants who are randomized are included in the statistical analysis and analyzed according to the group they were originally assigned, regardless of what treatment (if any) they received."

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April 19, 2021

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VIA EMAIL
Phil.fontanarosa@jamanetworks.org

Re: JAMA. 2013;309(20):2139-2149. doi:10.1001/jama.2013.5566

Dear Dr. Fontanarosa:

This letter is in response to the email from Dr. Howard Bauchner dated March 24, 2021, in which he requests a response from me, Dr. Christopher O'Connor, and two other authors of the above-referenced publication regarding the following topics:

1. Analysis of data collected during the study which was the basis for the above referenced published article with regard to the inclusion and exclusion criteria published in the original protocol[1]; and

2. IRB concerns about protocol deviations.

These responses will be provided in reverse order for reasons of clarity. In addition, I include a third section which points out several inaccuracies in the letter from Scott Compton regarding the participants he believes should be excluded from the data analysis.

IRB Re: Protocol Deviations

IRB documents pertaining to the REMIT study[1] are attached to this letter as Exhibit A[2]. These documents show that the IRB review of REMIT found **no concerns** about

[1] Jiang W, et al. Responses of mental stress-induced myocardial ischemia to escitalopram treatment: background, design, and method for the Responses of Mental Stress Induced Myocardial Ischemia to Escitalopram Treatment trial. Am Heart J. 2012;163:20-6.

[2] The IRB documents in Exhibit A include approvals during the REMIT study (2006-2011) and also those in response to the internal Duke audits during 2018-2019 initiated by Dr. Moira Rynn, who became head of the Psychiatry Department in 2017. Dr. Rynn has stated that she initiated the reviews of the REMIT study based on

the conduct of the study, data analysis, or patient safety.

As I informed Dr. Rynn, Dr. Compton, Duke IRB, and Duke SCMR in response to every internal Duke audit, the investigators amended the protocol to omit the eligibility requirements for temporary beta blocker discontinuation and/or required exercise stress testing due to patient safety considerations. If the patient was treated with beta blockers at baseline, the endpoint evaluation was also performed on beta blocker therapy.

The primary purpose of REMIT was the evaluation of mental stress-induced myocardial ischemic, Therefore, exercise stress testing was not required to evaluate the hypothesis. The beta blocker and exercise testing components were not necessary for the primary study objective and were taken into account in the analysis of secondary endpoints. Distinguishing MSIMI and exercise-induced myocardial ischemia is clinically and mechanistically relevant.

Finally, Duke IRB policy did not then and does not now require **prior** IRB approval for protocol amendments necessary to protect patient safety. See IRB policy "Amendments to Previously Approved Research," current as of 03.01.2016. In addition, see IRB policy "Problems or Events That Require Prompt Reporting to the IRB", (current as of 08.09.2019, (hereinafter IRB policies)[3]. See also 45 C.F.R. § 46.108(a)(4)(i) (reporting required for unanticipated problems involving risks to subjects) and 46.108(a)(3)(iii)(prompt reporting to IRB not required when necessary to eliminate hazards to subject); 21 C.F.R. § 56l.108(b)(1) (requiring IRB notification of unanticipated problems involving risks to subject in FDA regulated clinical investigations) (hereinafter CFR regulations).

The Psychiatry Department Clinical Research Unit (CRU) audited the REMIT study and found no patient safety concerns and no evidence of research misconduct. Notably, the REMIT study began in 2006 prior to any of the institutional requirements that the 2018 audit team applied to the study. The Duke Office of Clinical Research applied policies to the REMIT study that were adopted after 2011 and were not in effect at the time of the study. In addition, the CRU auditors acknowledged that it was "common to amend forms throughout the life cycle of a trial." The audit team also noted that during the REMIT study, Duke was transitioning from paper record-keeping which the REMIT study used in 2006, to electronic record keeping, which began during the conduct of the REMIT study.

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allegations she claimed she received from Pamela Bonner, my research coordinator who was with me between May 2017 to April 30, 2018, but Ms. Bonner denied making any allegations.

[3] Duke's IRB follows federal law under OHRP. https://www.hhs.gov/ohrp/sachrp-committee/recommendations/2012-march-30-letter-attachment-c/index.html- 79k- 2016-04-26

Dr. Rynn escalated the departmental audit to the Duke Office of Audit, Risk & Compliance (OARC). This OARC audit confirmed the findings of the department but did not identify any new concerns. Nevertheless, my laboratory manager and statistician, Stephen Boyle and I collaborated on a response which was submitted to the OARC on October 18, 2018, fully explaining the protocol changes alluded to above. In a meeting on November 13, 2018, with Greg Samsa and Donna Kessler of the Data Integrity Office, Stephen Boyle and I were also told the fact that the protocol implementation without formal IRB amendment submission was a common issue observed by the Duke Clinical Research Institute when reviewing clinical trials.

On December 26, 2018, the Duke IRB reviewed the OARC report and our response. They concluded that the audit identified no Unanticipated Problem Involving Risk to Subjects or Others (UPIRTSO). In addition, the IRB stated it could not provide an opinion on the data reporting without additional independent, expert review of the conduct of stress tests in relationship to the echocardiograms. The IRB stated that "**Dr. Jiang and her co-investigators** . . . **with the support of the CRU and School of Medicine**, should seek **independent expert opinion** on these issues and report back to the Board with their conclusions."

The IRB's recommendation for "independent" and expert" evaluation of the REMIT study was not followed by Dr. Rynn. Instead, Dr. Rynn directed the Psychiatry Department CRU to conduct **another** evaluation of the data collected and used in the data reporting. In keeping with the IRB recommendation for an independent expert evaluation, I decided to reach out to my co-investigator cardiologists to consult on obtaining such an evaluation. However, when I informed Dr. Rynn that I intended to reach out, Dr. Rynn essentially forbade me from doing so as Psychiatry Department chair.

The Duke IRB reviewed the **second** audit conducted by the Psychiatry Department CRU of the REMIT study and again determined that no UPIRTSO had occurred in December 2018.

In 2019, despite the consistency of multiple audits and reviews that found no significant concerns and the recommendation for an independent review of the trial, Dr. Rynn, escalated her allegations about the REMIT study to U.S. Health and Human Services (HHS) Office of Research Integrity (ORI) to conduct an inquiry into allegations of possible falsification of the REMIT clinical research records which would constitute professional misconduct. Falsification under ICMJE and COPE guidelines is quite specific as are the processes to be followed when suspected. In addition, falsification and fabrication imply intent to mislead. Dr. Rynn had no factual basis from any of the previous audits to suspect falsification under the ICMJE or COPE guidelines or any intent to mislead by the authors of the JAMA article.

Subsequently, Dr. Rynn commissioned the Duke Standing Committee on Misconduct in Research (SCMR) to conduct the evaluation for the HHS ORI inquiry. In March 2019, a statistical re-analysis of the primary REMIT study outcomes reported in the JAMA 2013 article was conducted by statisticians at the Duke Clinical Research Institute (DCRI). Again, this analysis was not "independent" as it was still internal to Duke and none of the SCMR evaluators were cardiologists (see Exhibit B). Moreover, the Duke Research Quality Framework policy specifically states that an **external, independent review** should be undertaken for research that is considered questionable or conflicted.

In September 2019, I met with Paul Lantos, Jody Power, and Walter Lee, Chairs of the Duke IRB to discuss the draft conclusions of the SCMR. Paul Lantos emailed me after the meeting on October 26, 2019:

> *"Thanks again for coming over to meet us. We acknowledge your concern about whether a reevaluation of the echo data from the REMIT study might cast doubt on your findings primarily due to advances in echocardiography in the years since REMIT was done.*
>
> *We hopefully provided some reassurance that this would be an unlikely outcome, as our goal is not to reevaluate 2006 science using 2019 eyes. There is really a spectrum of outcomes, with the extremes being that an audit fully confirms the original findings or it's completely incompatible with them. In between these two there could certainly be a gray area in which the original findings would be seen as reasonable. If it happens that the audit finds major fault with the original findings, I can't imagine that this would lead to a summary judgment or action without first diving deeper into these findings, and certainly making sure you and your collaborators aware.*
>
> *I believe that was the understanding we reached during the meeting. Please let me know if there is anything you believe I missed.*"

In addition, Dr. Lantos had previously confirmed in an email on October 19, 2019, that in his position on the IRB, he understood the IRB's "mandates" to be "subject safety, scientific integrity, and compliance with regulations and laws." He indicated that if an "incompatibility" was discovered between the original findings and the audit,

> *"our next step would be to figure out what it means, and it's hard to speculate before the audit is done. But I hope you'll see this as an opportunity to confirm your studies' validity in light of the audit and the enrollment concerns. We'll certainly keep you posted."*

On November 26, I again conferred with the Duke IRB chair Paul Lantos and also with Ombudsman Thomas Metzloff because I had serious concerns about the methodology of the re-analysis.[4] I again expressed my desire to consult with the REMIT cardiology co-investigators / collaborators who provided the original cardiology and statistical analysis due to their expertise in echocardiography. I explained that Dr. Rynn had instructed me NOT to reach out to the original study team because they were no longer at Duke, indicating again that she did not want any independent evaluation of the study.

Dr. Lantos emailed me and indicated that he "wanted to confirm, having spoken with Jody Powers, that the IRB would like the cardiologists who were on your study to have the opportunity to review and respond to the echo audit, even if they are no longer at Duke." In fact, Dr. Lantos had previous stated to me on November 26, 2019:

> *"My personal point of view is you did your science as a team and it should be the team that responds to an audit or investigation, especially for something like echo interpretation or statistics for which you have coinvestigators who are experts.*
>
> *I do not think we as the IRB have any authority to tell you whom you can or can't consult with, nor do we have the authority to override instructions from others to NOT speak with anyone.*
>
> *Tom will be able to answer this better than I, but I'm not sure you can really be prohibited from speaking with someone unless it's on the advice of Duke counsel or it's a case of protected information that can't be shared. It's worth contesting any instructions you've gotten to not speak with your collaborators if you feel they are unfair or against policy."*

In summary, with regard to Dr. Bauchner's original query regarding the position of the IRB on the conduct of the REMIT study, despite the fact that the various internal Duke reviews were not "independent" or "expert" as recommended by the IRB, none of the IRB reviews found any patient safety issues. As for the quality of the data analysis, the reviews were all fairly confirmatory of the original statistical analysis (as discussed below).

<u>Data Analysis regarding Inclusion/Exclusion Criterion</u>

Scott Compton and Moira Rynn have raised concerns about the analysis of data collected during the REMIT study. They believe that the JAMA article analysis

[4] A summary of the flaws in the re-analysis signed by REMIT study co-investigators and co-authors of the JAMA article is attached to this letter as Exhibit B.

should have excluded data from 26 of the participants because they did not meet the inclusion and exclusion criteria published in the original protocol[5]. On the other hand, I and the co-investigators are of the opinion that those participants must be included because the data analysis method used in the JAMA article was the most reliable ITT (intention to treat) method.

Specifically, the data was analyzed and reported in the JAMA article using the intention-to-treat (ITT) analysis[6] (McCoy 2017) because ITT data analysis allows the

> *investigator (or consumer of the medical literature) to draw accurate (unbiased) conclusions regarding the effectiveness of an intervention. This method preserves the benefits of randomization, which cannot be assumed when using other methods of analysis.*

Even if the statistical analysis done by the Duke DCRI statisticians is used, it is clear and in their own words that "the results obtained from this reduced patient sample are in general very similar to the results published in JAMA." (See Exhibit B). Specifically, the re-analysis shows a potential benefit of SSRI at 6 weeks. The OR is favorable, the p-value is no longer significant, but the trend aligns with the primary hypothesis. The number of subjects was below the original target and modest to the point that p-values are less impactful.

In addition, the method section of the original JAMA paper clearly states that ITT would be used. The primary outcome of presence of MSIMI at 6 weeks and its association with treatment assignment was examined under intention-to-treat (ITT) principle using logistic regression. We used multiple imputation techniques[7] to compensate for potential bias introduced by missing endpoint data. The imputed model to predict the outcome consisted of age, baseline resting EF, sex, and the treatment variable. For our primary outcome, unadjusted and adjusted imputed logistic regression models provided odds ratios and 95% confidence intervals (CIs) for the association of the study intervention with MSIMI. The Hosmer-Lemeshow statistic was reported as an index of goodness of fit for this model. For the primary outcome, per-protocol analysis was also conducted on participants who completed both baseline and endpoint assessments.

Inaccuracies in Letter from S. Compton

[5] See 1. For the reference of the REMIT method paper in American Heart Journal 2012.
[6] Understanding the Intention-to-treat Principle in Randomized Controlled Trials C. Eric McCoy, MD, MPHWest J Emerg Med. 2017 Oct; 18(6): 1075–1078. Published online 2017 Sep 18. doi: 10.5811/westjem.2017.8.35985 PMCID: PMC5654877 PMID: 29085540
[7] Schafer JL. Multiple Imputation: A primer. Statistical Method in Medical Research. 1999;8:3–15.

The number of protocol deviations in the REMIT study participants listed in Table 2 of Scott Compton's letter to JAMA (March 15, 2021) is incorrect.[8] Of the 26 REMIT subjects claimed by Scott Compton to be "ineligible," 7 of those individuals had no issues of protocol deviation; 19 REMIT subjects who were not able to comply with the temporary beta blocker withhold (N=11), with the exercise test (N=6), and with both (N=2). (See Exhibit C). Ultimately, they were approved for inclusion by the IRB in January 2019 and no UPIRTSO was found by the IRB (See Exhibit A).

Since the statistical analysis plan of the REMIT study for the primary study l was ITT, the p-values would have remained statistically significant as originally reported in the JAMA article.

Conclusion

My co-investigators (three of whom are copied below) and I continue to stand by our original article, with the exception of the very few typographical errors noted in my original letter to you on December 18, 2020. I urge you to reach out to us if you still have questions regarding either IRB approvals or the data analysis in the article.

Sincerely,

Jan Wei Jiang

Attachments: Exhibit A (IRB documents)
Exhibit B (Duke DCRI analysis excerpt)
Exhibit C (Jiang Response to IRB inquiry (via Scott Compton) re ineligible subjects

[8] Since January 2019, Scott Compton has been aware that the numbers of subjects he claims did not fit the protocol are incorrect because of the response I submitted to him and the IRB at that time.

cc: Annette Flanagin, MD (via email)
Executive Managing Editor

Christopher O'Connor, MD (via email)
Richard Sean Stack, M.D. Distinguished Professor/Duke University and President of Inova Heart and Vascular Institute

Richard C. Becker, MD (via email)
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